PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE

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Dedicated

to

my Family

&

Teachers

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ABBREVIATIONS

ADC	Apparent Diffusion Coefficient
BaFT	Barium follow through
CD	Crohn’s disease
CDAI	Crohn’s disease activity index
CC	Colonoscopy
CDEIS	Crohn’s disease endoscopic index of severity
CTE	CT Enterography
DCBE	Double contrast barium enema
DWI	diffusion weighted images
FISP	Fast imaging with steady state precision
FLASH	Fast Low Angle Shot
HASTE	Half Fourier acquisition single shot turbo spin echo
IBD	Inflammatory bowel disease
MRE	MR Enterography
MaRIA	Magnetic resonance index of activity
MEGS	Magnetic Resonance Enterography Global Score
SBE	Small bowel enteroclysis
SES- CD	Endoscopic Crohn’s disease index
US	Ultrasonography
VIBE	Volumetric interpolated breath hold examination

ABSTRACT

INTRODUCTION: MR Enterography has emerged as an important non-invasive radiation free modality providing simultaneous information about mural and extramural extent of inflammatory bowel disease and its complications, thereby dictating its diagnostic and prognostic value.

AIMS: 1. To evaluate the profile of MR Enterography in assessing the extent and disease activity in patients with Crohn's disease and correlate with clinical and endoscopic reference.

2. To assess the added advantage of diffusion weighted imaging sequence over conventional MR Enterography sequences.

METHODS: This prospective study was conducted on 32 Patients with clinically suspected or proven cases of Crohn's disease in department of Radiodiagnosis, Dayanand Medical College and Hospital. MRI parameters were used to document the disease activity and extent which were correlated with clinical and endoscopic reference.

RESULTS: The correlation of Crohn's disease activity index (CDAI) clinical scoring with Simple Endoscopic Score (SES-CD) and MRI scoring for disease activity were very weak and not statistically significant. The MR Enterography Global Score (MEGS) for disease activity showed a significant correlation with endoscopic (SES-CD) scoring (p value 0.007). MRI demonstrated a sensitivity of 92% and a specificity of 57.4 % with accuracy of 84.3% compared to colonoscopy. Correlation between Endoscopic and DWI scoring for disease activity was statistically significant (p value 0.03). Qualitative assessment of DWI has reasonable sensitivity of 92% in Crohn's disease based on a colonoscopic standard of reference but has poor specificity of 42.8% and cannot fully replace conventional sequences. The correlation between DWI scoring and MR Enterography Global Score (MEGS) for disease activity was statistically significant (p value 0.002).

CONCLUSION MRE demonstrates excellent sensitivity and moderate specificity compared to colonoscopic reference. The value of DWI may have an adjunctive role in the assessment of disease activity.

KEYWORDS: Crohn's disease, MR enterography, Inflammatory bowel disease, fibrostenotic, MEGS scoring, SES-CD, penetrating fistulizing.

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INTRODUCTION

Crohn's disease is a chronic inflammatory condition of the bowel, predominately affecting the young and requiring lifelong medical and often surgical therapy[1]. The incidence of Crohn's disease has a bimodal distribution as a function of age. The disease tends to strike people in their teens and twenties and people in their fifties through seventies. It is rare in early childhood.

The features of Crohn's disease (CD) differ between the early and chronic stages of the disease. Typically in the early stage of CD there are areas of focal inflammation with aphthoid ulcerations and lymphoid hyperplasia. These progress to longitudinal and transverse mucosal ulcerations and eventually the ulceration may become transmural. Thereafter complications may arise including strictures, sinuses, fistulae and perienteric abscesses. Histologically, the chronic inflammatory process is typified by non- caseating granuloma formation. In the chronic stage of CD, there is fatty infiltration of bowel wall and fibrofatty infiltration of mesenteric fat. When disease becomes chronic it is characterized by fibrosis and stricture formation.

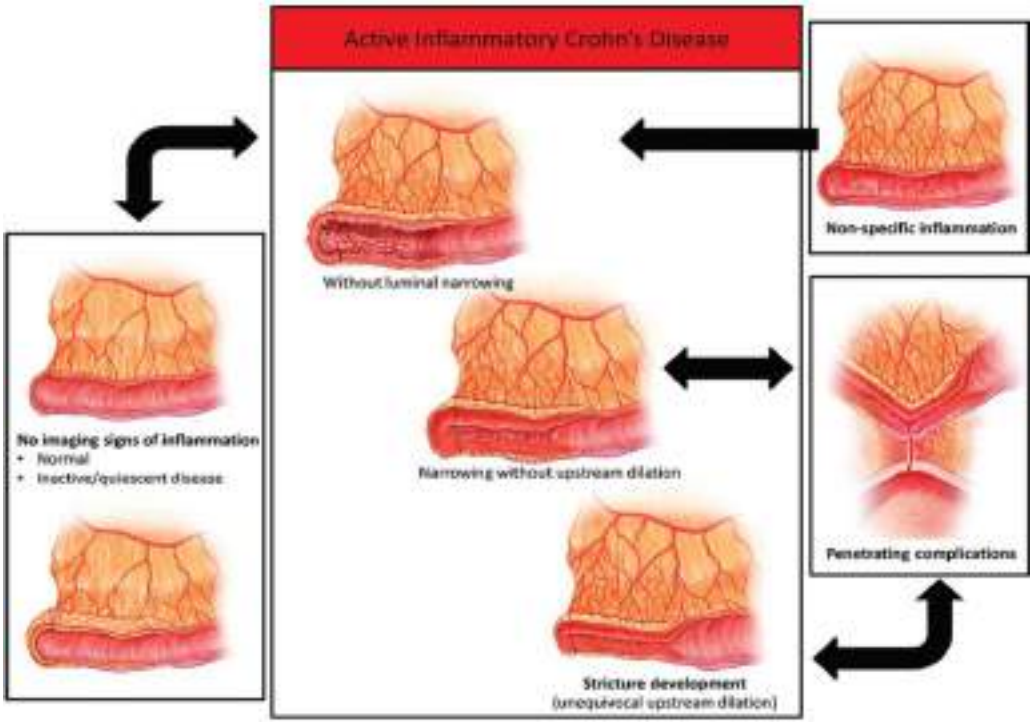

Figure 1 Pathogenesis of bowel inflammation in Crohn's disease. (adapted from source reference no 37)

Crohn's disease commonly affects terminal ileum and proximal colon although it can involve whole of gastrointestinal tract. Bowel involvement is segmental typically manifesting as "skip lesions".

The natural history of the disease is one of intermittent acute exacerbations characterised by an acute inflammatory response, separated by periods of relative quiescence. Medical therapy is based largely on immunosuppressive medication. Although relatively effective, these drugs are not without significant side effects, some of them life threatening, notably sepsis secondary to immunosuppression. Furthermore therapeutic agents such as anti- TNF are expensive and often require intravenous administration. Rational use of immunosuppressive therapies in inflammatory bowel disease (IBD) therefore relies on accurate identification of those patients with acute inflammation –so called "active disease", who are most likely to respond to the treatment, together with assessment of the disease extent.

The management of IBD and assessment of response to medication largely depends on accurately documenting the location, extent and the severity of the inflammation[2,3]. Unfortunately there is no single reliable non-invasive method to identify such patients.

Clinical assessments based on patient symptomatology (such as the Crohn's disease activity index) are relatively subjective [4], and patients with inactive disease (such as those with chronic fibrotic strictures) often attract high scores. Biochemical markers such as ESR and CRP are useful adjuncts [5] but again do not in themselves always differentiate reliably between active and chronic disease.

For those patients with ileocolonic disease, conventional endoscopic techniques allow direct visual inspection of the mucosa and is an essential tool for diagnosis, management and prognostic evaluation of inflammatory bowel disease [6]. However it is invasive, often uncomfortable and patients are often reluctant to undergo the necessary repeat procedures over the course of their disease. Furthermore in those with colonic stricturing disease, complete colonoscopy may be impossible.

Radiological investigations such as barium fluoroscopy provide useful information about the small bowel, but give little information about disease in the colon, and involve relatively high doses of radiation [7], which is problematic for young patients with chronic disease. Endoscopic features do not always correlate with clinical and biochemical markers [8]. Furthermore, they provide little information regarding extramural manifestations such as abscess formation, which can be of great importance in patients being considered for strong immunosuppression. Although the incidence of perforation after endoscopic procedures is low, it is very well recognized [9].

Radiological assessment can be performed using both barium enema and CT. Both techniques expose patients to ionizing radiation. Although barium enema facilitates assessment of relatively early mucosal disease, CT enterography provides information on both mural and extra mural disease. [10, 11].

Magnetic resonance imaging has been advocated as a potentially useful investigation for assessment of those with IBD without exposing patients to ionising radiation [12-14]. It images the whole bowel, providing simultaneous information about mural and extramural complications. Furthermore it has also been suggested that specific enteric and mesenteric appearances on MRI (such as bowel wall signal and contrast enhancement, lymphadenopathy, mesenteric high signal) are related directly to disease activity [15,16] and as such may help rationalise the use of, and monitor response to immunosuppressive therapy.

The thesis examines the use of magnetic resonance Imaging (MRI) in Crohn's disease. A qualitative MRI scoring system of severity proposed and tested against current clinical indices and patient outcome. The ability of MR enterography to assess disease activity in the colon against an endoscopic standard of reference is then addressed using qualitative MRI scoring systems.

ASSESSMENT OF CROHN'S DISEASE

IBD is a lifelong condition and patients must undergo repeated examinations to assess current disease extent and activity. It is therefore important that such examinations cause as little disruption, risk and discomfort to patients as possible. Even now, there is not one simple test that fulfills all the needs of the clinician in assessing patients with IBD and gastroenterologists in routine practice use combination of clinical assessment, numeric clinical indices, endoscopic findings and imaging modalities for this purpose.

a. **Clinical activity scores - Crohn's disease activity index (CDAI)**

Although the CDAI is one of the most commonly used clinical indices particularly in the context of clinical trials it has undoubted limitations including

- Interobserver variability of symptom reporting between patients
- High weighting of scores of "general well being" and intensity of 'abdominal pain'- which are subjective.
- The calculation requires diary keeping by patients for 7 days, compliance is an issue in every day practice.
- Misleading results in fistulating and stenosing disease.
- Limited utility in patients with previous ileo- colic resection and stoma.

b. Biochemical Markers of activity

The ideal biochemical marker in IBD should be helpful in identifying patients at risk, should be disease specific, should be able to monitor disease activity and should be minimally invasive. The most common biochemical markers are Erythrocyte sedimentation, C-Reactive Protein, Total Leucocyte Count and platelets, Fecal Calprotectin.

c. Colonoscopy

The endoscopic features of IBD include friable mucosa, spontaneous bleeding, aphthoid ulcerations, cobblestone appearance and stenosis [17].

The advantages are as follows:

1. Endoscopy provides exquisite images of the enteric mucosa

2. It is regarded as the most accurate modality for the assessment of the extent and the severity of disease.

The disadvantages are as follows:

1. It is unable to visualize the small bowel beyond terminal ileum.

2. Luminal stenosis may also limit endoscopic examinations.

3. Endoscopic features do not always correlate with clinical and biochemical markers [8].

4. Although the incidence of perforation after endoscopic procedures is low, it is very well recognized [9].

5. Patient experience of colonoscopy may be somewhat negative with the rigors of bowel preparation, procedural discomfort, and embarrassment[18].

Various scoring endoscopic scoring systems for assessing disease severity and activity have been developed over time, notably the Crohn's disease endoscopic index of severity (CDEIS), Simple Endoscopic Crohn's disease index (SES-CD) and Rutgeert's score.

d. Barium Fluoroscopy

Small bowel enteroclysis (SBE) and small bowel follow through (SBFT) are the traditional radiological techniques used for assessment of small bowel morphology. Both enable direct visualization of bowel lining, width of lumen and stenosis, range of affected segments and presence of complications. In experienced hands, they have similar sensitivity of 85-95% and specificity of 89-94% in detecting radiological signs of CD [19]. Only assessment of the lumen is generally achieved and transmural extension of CD and extra luminal complications are usually missed. The technique also uses ionizing radiation with total effective dose up to 10.7 mSv from a single examination [20,21].

e. Ultrasonography in IBD

Ultrasonography is easily accessible, inexpensive, non-invasive, painless diagnostic tool with the potential widespread clinical use due to ubiquity of ultrasound equipment. It provides information about mural and extramural manifestations of disease – fibrofatty

proliferation, enlarged lymph nodes, abscess or fistulae [22-24].

Jejunal or duodenal disease is often missed using US, while the rectum and distal sigmoid are not visualized fully due to their pelvic location [25-27]. It is extremely operator –dependent. It is difficult to perform on overweight patients as adipose tissue attenuates the ultrasound beam.

f. CT Enterography (CTE)

CT Enterography and CT Enteroclysis are modification of conventional CT technique optimized for the evaluation of small bowel by administration of large volume of enteric contrast agent either orally (CT Enterography) or through a nasojejunal catheter (CT enteroclysis).

In suspected cases of IBD CTE has sensitivity of 83% in comparison to SBE and 80- 88% compared to endoscopy . For detection of disease and in cases of known IBD it has a sensitivity of 80-90% and specificity of 90-98% in comparison to endoscopy, SBE and surgery. In general CT is not accurate in detection of early superficial lesions [28].

g. MR ENTEROGRAPHY IN CROHN'S DISEASE

MRI evaluation of the small bowel typically combines large volume enteric contrast distention of bowel with rapid breath hold T2 and post contrast T1 weighted images in the axial and coronal plane [29]. Bowel distension is in general a pre-requisite to enteric MRI. By distending the bowel, it is possible to evaluate the inner and outer borders of the bowel wall and much better appreciate wall thickening, abnormal enhancement and mural signal changes. Inadequate distension is one of the most common causes for failed MRI Enterography.

With its ability to assess disease activity and distribution, and diagnose complications such as obstruction, perforation, strictures and abscesses, MRI of the small bowel is increasingly indicated for first diagnosis of IBD, suspected disease relapse, assessment of treatment failure and before planned surgical resection [30].

MR enteric contrast agent is administered either orally (MR Enterography) or through nasojejunal tube (MR Enteroclysis).

Enteric findings

Typical features of Crohn's disease include [31-34]

a. Thickening of wall of diseased segment

Wall thickness more than 3 mm in distended small bowel loop is abnormal, it usually ranges between 5-10mm and is accurately assessed with HASTE sequences. Wall thickness is usually greater in CD as compare to UC due to transmural inflammatory process.

b. Abnormality in mucosal folds

- Picket fence pattern of diffusely thickened folds
- Reduction or distortion of folds due to ulceration
- Cobblestoning- a patchy areas of both high and moderate signal intensity caused by longitudinal and transverse ulceration seen on true FISP images

c. Ulcerations

Moderate to deep ulceration can be seen as thin lines of high signal intensitywithin thickened bowel wall on HASTE images.

d. Strictures – with segment of thick wall

A stricture is an area of luminal narrowing in a diseased bowel loop with unequivocal upstream dilation

When multiple pulse sequences, fluoroscopic observation, or serial imaging exams demonstrate fixed narrowing without upstream dilation, it is appropriate to describe that a **probable stricture** is present

e. Wall edema

High T2 signal intensity particularly well seen on fat saturated images.

f. Mural enhancement

-Stratified or layered pattern- bright mucosa due to inflammation and hypoenhancing submucosa due to edema.

-Diffuse pattern- homogeneous enhancement of entire wall thickness dueto transmural inflammation

-Low –level inhomogeneous enhancement- likely represent fibrosis

g. Pseudosacculation or Pseudodiverticulum

Fibrosis and shortening of diseased mesenteric wall cause dilatation of antimesenteric border [35].

Extraenteric findings

a. Comb sign [36]

Short low- signal intensity parallel lines on true FISP images and as high signal intensity lines on VIBE images due increased mesenteric vascularity during active disease.

b. Mesenteric edema

It is seen in advanced active disease. Increased mesenteric signal best seen on fat saturated T2 weighted images.

c. Fat wrapping/ hypertrophy

Increased mesenteric fat causes displacement of mesenteric vessels or other viscera. It is a specific sign of CD, representing long standing transmural inflammation.

d. Lymph nodes

Hyper enhancement, enlargement and edema of lymph nodes adjacent to bowel seen on fat-saturated HASTE and True FISP images

e. Fistulas and sinuses

Seen as high signal intensity tracts on T2- weighted images or as enhancing tracts on post contrast enhanced T1 weighted sequences e.g. enterocolic, enteroenteric or enterocutaneous.

f. Abscess

As well defined, encapsulated collection of pus with high signal intensity on T2 – weighted and low signal intensity on T1 – weighted images typically with an enhancing rim [31].

MRE-based indices for quantification of bowel inflammation

Many studies have focused on developing indices for quantification of active disease which will help in guidance of patients' therapy. MRE indices serve as a disease quantification tool and thus may help standardize measured outcomes in clinical trials of treatment interventions for CD. In addition, these indices may be used in academic research and when validated may provide a quantified clinical decision tool for estimating mucosal healing. The most commonly used indices [37] are as follows-

1. Magnetic resonance index of activity (MaRIA)

The MaRIA is the most studied index and offers an extensive data of its performance against different investigating modalities (clinical scores, pathology, conventional endoscopy, video capsule endoscopy, inflammatory biomarkers). Therefore, it may be considered for use as a reference index these days.

2. Magnetic Resonance Enterography Global Score (MEGS)

The MEGS lacks pathological validation but on the other hand is correlated with clinical score of disease activity, stool and blood markers. It has the advantages of evaluating the entire small bowel and incorporating extra-intestinal findings and should be used as a tool for evaluating the extent of the disease. Of note is that the MEGS score is complicated to obtain, due to its large number of variables. MRE gained great popularity over the years and is considered one of the gold standards for the diagnosis and follow up of CD.

AIMS AND OBJECTIVES

1. To evaluate the profile of MR Enterography in assessing the extent and disease activity in patients with Crohn's disease and correlate with clinical and endoscopic reference
2. To assess the added advantage of diffusion weighted imaging sequence over conventional MR Enterography sequences.

REVIEW OF LITERATURE

Over the time, significant amount of work has been undertaken regarding use of MRI (enterography & enteroclysis). Diagnostic accuracy of MRI has been compared to various reference standards and below is the summary of some of these.

Endoscopic Reference

Magnano and colleagues compared MRE, US and Doppler US using ileocolonoscopy asreference standard in children with known CD. MRE was performed after oral intake of polyethylene glycol solution. It depicted stenosis, thickening and hyperemia of bowel wall. Concordance of MR and US for detection of wall thickening and increasedvascularity was 95% and 80% respectively [38].

Florie et al [39] used water as intraluminal contrast medium and compared MRI with endoscopic grading of disease severity -CDEIS. Wall thickness correlated moderately to strongly with CDEIS ($r=0.57, p<0.001$ and $r=0.50, p<0.001$) while enhancement correlated weakly to moderately ($r=0.45, p<0.001$ and $r=0.42, p<0.001$). They also compared patient experience and overall preference. Patients found endoscopy more painful and hence, expressed preference for MRE as future investigation. In the same year, another study of MRE was performed at 3.0 T MRI and also used CDEIS as standard of reference [40]. Only a weak to moderate correlation was found between bowel wall thickness and CDEIS and between wall enhancement and CDEIS. Again the majority patients preferred MRE to ileocolonoscopy.

Borthne and colleague [41] compared the sensitivity, specificity and diagnostic accuracy of MRE (300 mL mannitol in 15% water) and US to endoscopy in children with suspected IBD. They assessed wall thickness and contrast enhancement and found sensitivity of 81.8%, specificity 100% and diagnostic accuracy of 90% for MRE for CD. 50% of patients were willing to repeat the examination in future.

Diagnostic accuracy of MRE has also been compared to wireless capsule endoscopy (WCE). In one such study, Golder and colleagues detected the same number of inflammatory lesions in terminal ileum

with both modalities but WCE detected additional lesions in proximal ileum and jejunum (12 vs. 1) whereas, MRE showed extra intestinal pathologies in 28% [42]. Two years later, Tillack et al [43] also compared MRE with WCE but only in known patients with CD. Both modalities showed the same disease features in 56% segments but WCE detected more superficial mucosal disease. However, MRE was better in diagnosing severe inflammatory mural changes.

Sailer et al proposed an MRE score for post surgical recurrence, based on image quality, contrast enhancement, mural and extra mural bowel wall changes to assess post resection recurrence in CD.

MR0	No abnormal features
MR1	Minimal mucosal changes
MR2	Diffuse aphthoid ileitis, moderate recurrence
MR3	Severe recurrence with trans and extramural changes

Table 1 MRE score by Sailer et al.

They used the previously validated Rutgreets score as a reference standard and high agreement was observed between MRE score and Rutgreets score [44].

The ability of MRE to precisely detect active small bowel disease has been compared with CTE by using endoscopy as reference standard. In one such study in 2009, [45] a similar sensitivity of 90.5% for MR enterography and 95.2% for CT enterography (p 0.32) was reported for detection of active disease and both modalities diagnosed additional disease in 24% of patients who had normal ileocolonoscopy. A few years later, Fiorino and colleagues [46] again used ileocolonoscopy as reference standard to compare both modalities and reported supremacy of MRE in the recognition of strictures (p=0.04).

Non endoscopic Reference

Several studies have used, non-endoscopic standards of reference, MRE being compared to various biomarkers and other imaging modalities in children as well as adults.

Schunk et al compared bowel wall enhancement on MRI after oral administration of 1L of 2.5% mannitol with CDAI and CRP and reported superiority of MRE in distinction of active and inactive stenosis [47] which is crucial in planning of treatment.

In the same year Miao et al [48] compared MRE with oral water with US against a combination of clinical assessment, endoscopy, barium study or surgery as reference standard and found equivalent sensitivity in detection of active disease (87%).

Laghi et al [49] derived an MRE score based on wall thickness and contrast enhancement in children with known CD use CDAI as a global reference standard together with ileocolonoscopy to evaluate disease activity in terminal ileum. They used polyethylene glycol as the oral agent. This score exhibited sensitivity of 84% and specificity of 100% for recognition of erosive ileitis seen on endoscopy.

Pilleul et al [50] in 2005 again verified positive correlation between bowel wall thickness and pediatric CDAI on MRE with 5% mannitol but no significant correlation was established with contrast enhancement. MRE also revealed fistulae,strictures, intussusception in these patients.

The role of dynamic contrast MRE to distinguish between active disease and remission was evaluated by Pupillo et al [51]. They observed early and intense uptake of contrast which increased over time until a plateau was seen in diseased segments of bowel while in segments with remission uptake was less intense, although, still higher than normal segments. A significant correlation was reported between the peak of contrast uptake and CDAI.

Taylor et al [52] also used dynamic contrast enhanced MRI to correlate with histopathological markers of inflammation and angiogenesis. Patients had pre operative MRI and slope of contrast enhancement, time to maximum enhancement, enhancement ratio, the volume transfer coefficient K (trans) and extracellular volume fraction v (e) for

the diseased segment of bowel were measured and the resected specimen was re imaged. Acute and chronic inflammation scores and micro vascular density (MVD) were measured in resected specimen. They found a positive correlation between disease chronicity and enhancement ratio (correlation coefficient 0.82, p= 0.002) but negative correlation between slope of enhancement and MVD (correlation coefficient -0.86, p<0.001), supporting the hypothesis of increased micro vessel permeability with disease chronicity and an inverse relation of tissue MVD to mural blood flow.

In 2009 Martinez and colleagues [53] compared MRE (sodium phosphate and water) and Doppler US with clinical scoring and biological tests. Contrary to the previously reported equivalent sensitivity of MRE and US for detection of active disease in 2002, they found US was more sensitive in localization of diseased segment (91%/83%) although grades of hyperemia and contrast enhancement on MRE were higher in patients with clinical-biological active disease, in comparison to patients without clinical –biological activity (p=0.019,p-0.023).

Zappa and colleagues in a retrospective study [54] compared the mural and extra mural findings of pre operative MRE with the pathological analysis in resected specimen in 53 known patients of CD. The MRE parameters significantly associated with inflammation were wall thickness, wall enhancement, enhancement pattern, T2 relative hyper signal, blurred wall enhancement, comb sign, fistula and abscess.

Combined Endoscopic and non endoscopic reference

Low and colleagues used multiple reference standards including surgical, endoscopic and histological findings together with barium studies to compare MRI and CT. MRI was performed with 2% oral barium sulfate, rectal water and IV gadolinium while IV contrast enhanced CT was performed with positive and negative enteral contrast in equal number of patients. Based on wall thickness and contrast enhancement on MRE was found superior to CT in depicting disease (85% vs. 65% abnormal segments). It was not only better in depicting mild disease (79% vs. 49% segments) but also in delineating

mural thickening (41% vs. 11% segments) and mural enhancement (89% vs.11% segments) [55].

Koh et al [56] assessed bowel wall thickness, contrast enhancement and perienteric changes on MRE (with oral water) in comparison to CDAI, endoscopy and surgery. MRE had overall sensitivity of 91% and specificity of 71% on per patient basis while CDAI had sensitivity of 92% and specificity of 28% for active disease.

Thirty patients [57] with established CD underwent ileocolonoscopy (24 procedures) or double-balloon endoscopy (DBE) (10 procedures) after MR enterography on the same day. Two gastroenterologists and two radiologists who were blinded to the results of another study evaluated endoscopy and MREC findings, respectively. In colonic lesions the sensitivities of the MR for deep mucosal lesions, all CD lesions, and stenosis were 88.2, 61.8, and 71.4%, respectively, while the specificities were 98.1, 95.3, and 97.7%, respectively. In small intestinal lesions, MREC sensitivities for deep mucosal lesions, all CD lesions and stenosis were 100, 85.7 and 100% respectively while specificities were 100, 90.5, and 93.1%, respectively. Endoscopic scores were significantly correlated with MREC scores. Eleven (46%) of the 24 patients who were clinically not suspected to show stricture were observed to demonstrate stricture by radiologists. The results demonstrated that MRE can simultaneously detect the CD lesions of the small and large intestine.

The ability of T2 weighted images to detect disease has been compared to contrast enhanced T1 weighted sequences. In such an attempt, Maccioni [34] compared the diagnostic accuracy of oral contrast enhanced T2 weighted imaging with T1 weighted gadolinium enhanced imaging using endoscopy, small bowel barium, CT, US and clinical biochemical scoring as references. The authors recommended combined use of T2 and T1 weighted imaging achieved better diagnostic accuracy.

After establishing diagnostic accuracy for IBD, further steps have been taken to gauge capacity of MRE to distinguish CD and UC. Horsthuis in 2010 reported superior diagnostic accuracy of MRE in children for

CD than UC [58] against the reference standard of (esophagogastroduodenoscopy & ileocolonoscopy) and barium enteroclysis.

Enterography vs. Enteroclysis

MR enteroclysis although more invasive than MRE has shown promising results. Holzknecht et al [13] used oral magnetic particles in 18 patients with known CD before surgical intervention and showed a sensitivity of 95.8-100% for primary diagnosis of CD, 94.7% of stenosis and 100% for fistulae not to mention detection of complications such as abscesses and affection of ureter. Both MRI techniques have compared in suspected as well as known patients with CD. Negaard et al [59] compared MRE (6% mannitol) and MREnteroclysis (polyethylene solution) in patients with suspected CD. They evaluated bowel distension, wall thickness, contrast enhancement, detection of ulcers, stenosis and edema. Bowel distension was better with MR enteroclysis although both had high diagnostic accuracy. MRE and MR enteroclysis both showed sensitivity of 88%, specificity of 89/84%, positive predictive value 89/82% and negative predictive value of 89%. The authors also compared patient experience of both modalities and found higher patient preference for MRE due to less abdominal pain and discomfort [60].

Masselli et al also reported better jejunal distention ($p < 0.01$) and detection of bowel wall abnormalities ($p < 0.01$) with MR Enteroclysis but MR enterography was more acceptable to patients [61].

MRI vs. Barium Studies

For years Barium studies have been the standard radiological investigation for assessment of the small bowel morphology. A well performed barium enema can detect very early mucosal changes such as aphthous ulceration and when it comes to differential diagnosis of CD and UC, it has sensitivity of 95-98% [62].

In 2000, Rieber et al [31] compared conventional Barium enteroclysis and MR enteroclysis in 84 patients with histological and endoscopy correlation using wall thickness and detection of stenosis as diagnostic criteria. They reported a higher sensitivity and specificity with MR

Enteroclysis 92.2% vs. 85.4% and 92.6% vs. 76.9% respectively. No abscesses were detected on SBE and only 17.7% fistulae were seen while 77.8% fistulae and 17.8% abscess were detected on MRE.

Bernstein el al [63] compared the findings of SBFT and MR enterography with oral 2% barium sulfate and IV gadolinium in known CD patients and found similar findings in majority of patients. SBFT showed additional strictures and fistulae in four patients while MRE showed additional information regarding active inflammation in stricture areas like wall enhancement, vasa recta changes and lymphadenopathy in 8 patients.

Detection of proximal ileal disease is crucial because it is inaccessible on ileocolonoscopy. Ochsenkuhn and colleagues [64] reported superiority of MRE over SBE of MRE for this purpose as well. Using features including wall thickness, contrast enhancement and detection of stenosis, they diagnosed proximal ileal disease in 22 of 25 patients whereas SBE was only able to reveal disease in 4 of these patients.

A year later, Albert et al [65] not only compared MRI with double contrast fluoroscopy and capsule endoscopy at the same time. Small bowel Crohn's disease was diagnosed in 78% (MRE), 33% (Barium) and 93% (WCE) but again MRI was superior in identifying transmural CD and extraluminal lesions and exclusion of strictures.

Lee and colleagues [66] compared the accuracy of MRE, CTE and SBFT while using ileocolonoscopy as reference standard for small bowel inflammation and imaging studies and surgery and physical examination for extraenteric complications. They found 100% sensitivity for both MRE and CTE in comparison to just 37% for SBFT for detection of extra enteric complications. Therefore, they presented MRE as effective and radiation free diagnostic tool for disease assessment in IBD.

Rimola et al.[67] proposed and validated a simplified Magnetic Resonance Index activity score that appeared to be a very good tool for assessing the disease activity, permitting a proper patient classification into three groups: inactive, mild, moderate to severe in ways that closely mimic the endoscopic score.

MATERIALS AND METHODS

7.1 Source of Data

A prospective study was done on patients of clinically diagnosed Crohn's disease referred for MR Enterography to department of radiodiagnosis, DMCH, Ludhiana over a period extending from 1 Dec,2019 to 31 May,2021.

7.2 METHOD OF COLLECTION OF DATA

Written consent was obtained from each patient after explaining the procedure in his/her vernacular language to allay fear and anxiety. A detailed relevant history about onset, duration, nature and frequency of abnormal bowel habits and abdominal complaints was recorded in a pre-designed performa. Record of previous imaging, biopsy, endoscopic and biochemical investigations was evaluated for overall correlation.

Patients were subjected to a multiplanar, multisequential MRI scan of prepared bowel on a MAGNETOM SKYRA 48 channel 3 TESLA MR Machine by Siemens, Germany.

INCLUSION CRITERIA:

Patients with clinically suspected or diagnosed Crohn's disease with isolated terminal ileal involvement on colonoscopy.

EXCLUSION CRITERIA

- Patients with high grade bowel obstruction.
- General contraindications to MRI (cardiac pacemaker, metallic implants, severe claustrophobia, cochlear implants).
- Patients with history of contrast allergy or renal impairment.
- Patients who do not consent to be a part of the study.

PREPARATION OF THE PATIENT

The patients were asked to come after 4 hrs fasting. On arrival at the radiology department, patient will be asked to drink 800 ml PEG solution over 50 min.

Polyethylene glycol (PEG LEC) solution was prepared by dissolving PEG with electrolytes & flavoring agents (pineapple and orange) which is commercially available as PEG LEC 137.15 grams of powder in 2

litres of water. The oral contrast material was divided into two portions, and instructed to drink each portion in 25 minutes. To opacify stomach and duodenum just before imaging, patients were instructed to have another 200 ml of oral contrast. Patients were instructed to drink the solution gradually for even distension of the entire small bowel.

One hour after the commencement of oral contrast ingestion patient were imaged on **MAGNETOM SKYRA 48 channel 3 TESLA MR Machine by Siemens, Germany** using phased array abdomen coil in supine position. Patient will be instructed for breathing instructions.

After running the kinematic sequences and just before iv contrast enhancement sequences 1mg of i.v buscopan each was given to minimize movement artifact from peristalsis. Images were obtained.

TABLE 2 Magnetic resonance imaging protocol:

Sequences/ Parameters	Acquisition Time (sec)	Orientation	Resolution Matrix	FoV Read	FoV Phase	Number of slices	Slice thickness (mm)	Slice gap (mm)	Repetition time (msec)	Echo time (msec)	Flip angle (deg)	Fat suppressionn	Flow compensation	averages
Localizer	18	transversal coronal	179*256	430	100	15	6	9	1200	91	160	No	No	1
T2 coronal	175	coronal	288*320	300	100	35	5	0	2000	91	160	No	No	1
TriFi coronal	19	coronal	256*256	377	100	34	5	0	570	1.68	52	No	No	1
Cinematic TruFi	16	coronal	289*288	380	100	3	3	0	523	1.86	60	No		1
TruFi axial	19	axial	206*256	380	80.5	50	5	0	382.48	1.68	50	No	No	1

T2 axial	60	axial	203*320	331	78.1	35	5	1	1600	95	160	No	No	1
T2 Fatsat axial	60	axial	203*320	331	78.1	35	5	1	1600	95	160	No	No	1
VIBE Dixon coronal pre and post gard arterial portal venous	18+18	coronal	234*320	426	81.3	144	1	0	4.23	1.35	9	Yes		1
T1 VIBE Axial	15	Axial	182*320	380	81.3	72	3	0	3.31	1.3	9	Yes		1
DWI with b value of 50, 400, 800	232	transverse	108*134	380	80.6	30	5	2.5	5700	48		Yes	1	

MRI IMAGE ANALYSIS

The MR images were evaluated for mural and extramural findings

EVALUATION ON MRI FOR MURAL FINDINGS

Wall thickness, T2 signal , wall enhancement grade and pattern, DWI signal, length and number of segments of bowel involvement and hautral loss are evaluated on MRI images

a. T2 signal

On fat sat T2 weighted images mural T2 signal is graded as 0,1,2,3

Grade 0 equivalent to normal bowel wall

Grade 1 dark grey on fat saturated images

Grade 2 light grey on fat saturated images

Grade 3 areas of high signal approaching that of luminal contents

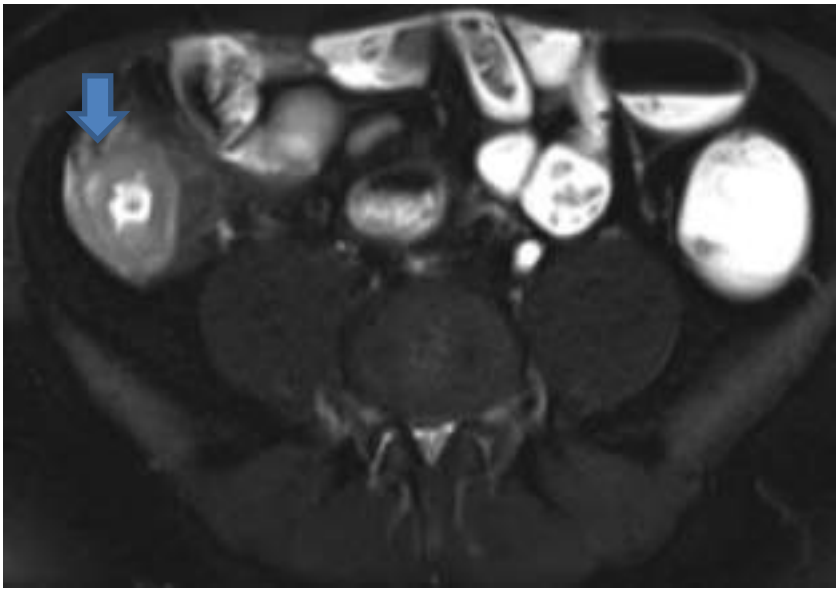

Fig 2 High signal intensity of diseased bowel on T2FS images

b. Mural thickness

On T2 weighted images mural thickness is graded as follows

Grade 0 <3mm

Grade 1 3-5mm

Grade 2 5-7 mm

Grade 3 >7mm

c. Mural enhancement on T1

Grade 0 Equivalent to normal bowel wall

Grade 1 bowel wall signal greater than normal small bowel but significantly less than nearby vascular structures

Grade 2 bowel wall signal increased but somewhat less than then nearby vascular structures

Grade 3 bowel wall signal approaches that of nearby vascular structures

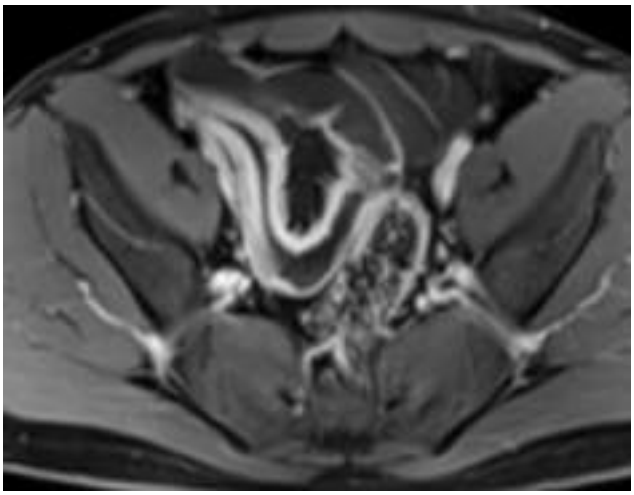

Fig 3 Grade 3 mural enhancement on post contrast images

d. Mural enhancement pattern

Grade 0 N/A or homogeneous

Grade 1 Mucosal

Grade 2 Layered/ Stratified

Grade 3 -------

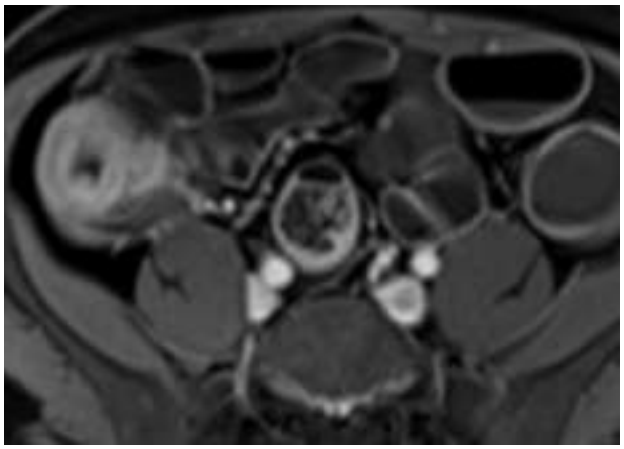

Fig 4 Stratified mural enhancement

e. Haustral loss

Grade 0 None

Grade 1 <1/3 segment

Grade 2 1/3–2/3 segment

Grade 3 >2/3 segment

f. Length of disease segment

Multiplication factor is added for MEGS score calculation as follows

×1: 0–5 cm

×1.5: 5–15 cm

×2: >15 cm

g. DWI signal

Visual assessment of the DWI data is done and graded on a 4 point scale with reference to normal bowel

Grade 0 normal

Grade 1 probably normal

Grade 2 probably abnormal

Grade3 abnormal

h. Skip segments

Involvement of skip segments is specific to crohn's disease.

i. Ulcerations

Moderate to deep ulceration can be seen as thin lines of high signal intensity within thickened bowel wall on HASTE images.

Segmental MEGS Score is calculated by adding grades for T2 signal, mural thickness, perimural T2 signal, T1 enhancement, mural enhancement pattern and haustral loss.

The scores for lymph nodes and comb sign were excluded from the individual segmental scores given the endoscopic standard was based on luminal evaluation only.

The maximum possible segmental score was 34 and graded as grade1 (5-15), grade 2 (15-25) and grade 3 (25-34).

Mural thickness

Grade 0 <3 mm

Grade 1 3–5 mm

Grade 2 5–7 mm

Grade 3 <7 mm

Mural T2 signal

Grade 0 Equivalent to normal bowel wall

Grade 1 bowel wall appears dark grey on fat-saturated images

Grade 2 bowel wall appears light grey on fat-saturated images

Grade 3 bowel wall contains areas of white high signal approaching that of luminal content

Perimural T2 signal

Grade 0 Equivalent to normal mesentery

Grade 1 Increase in mesenteric signal but no fluid

Grade 2 Small fluid rim (⩽2 mm)

Grade 3 Large fluid rim (⩾2 mm)

T1 enhancement

Grade 0 Equivalent to normal bowel wall

Grade 1 bowel wall signal greater than normal small bowel but significantly less then nearby vascular structures

Grade 2 bowel wall signal increased but somewhat less than then nearby vascular structures

Grade 3 bowel wall signal approaches that of nearby vascular structures

Mural enhancement pattern

Grade 0 N/A or homogeneous

Grade 1 Mucosal

Grade 2 Layered

Grade 3 -------

Haustral loss

Grade 0 None

Grade 1 <1/3 segment

Grade 2 1/3–2/3 segment

Grade 3 >2/3 segment

Multiplication score per segment

Length of disease segment

×1: 0–5 cm

×1.5: 5–15 cm

×2: >15 cm

Additional score per patient

Lymph node (1 > cm)

0: Absent

5: Present

Combs sign

Abscess

Fistula

Total score:

Score per segment X multiplication score per segment (jejunum, ileum, terminal ileum, cecum, ascending, transverse, descending, sigmoid and rectum based) + **additional score per patient** (lymph node + comb sign + abscess + fistula)

Table 3 MEGS calculation (table adapted from source[37])

EVALUATION ON MRI FOR EXTRAMURAL FINDINGS

a. Comb sign

Short low- signal intensity parallel lines on true FISP images and as high signal intensity lines on VIBE images due increased mesenteric vascularity during active disease.

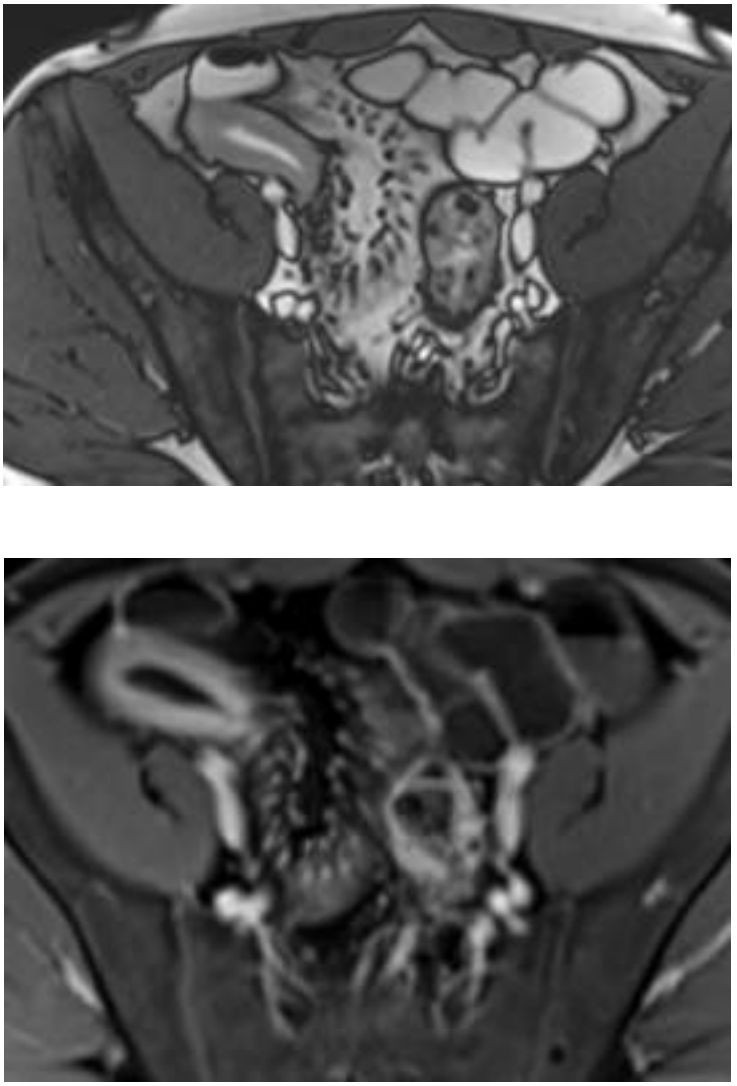

Fig 5A and 5B Comb' sign on TRUFI and post contrast images

b. Mesenteric edema

It is seen in advanced active disease. Increased mesenteric signal best seen on fat saturated T2 weighted images

Perimural T2 signal is graded as follows

Grade 0 Equivalent to normal mesentery

Grade 1 Increase in mesenteric signal but no fluid

Grade 2 Small fluid rim (⩽2 mm)

Grade 3 Large fluid rim (⩾2 mm)

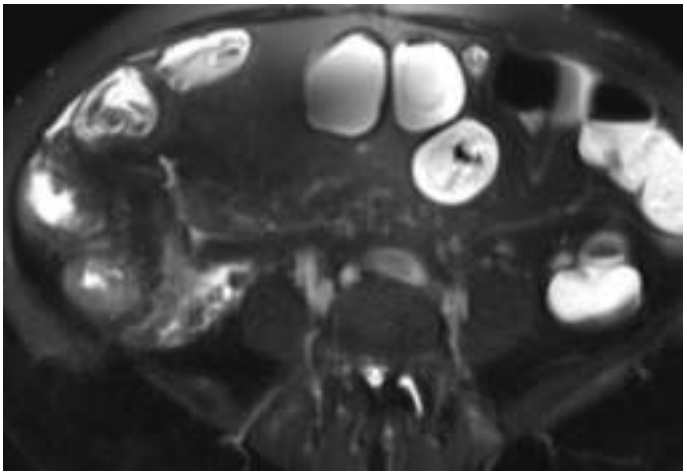

Fig 6 grade 3 perienteric changes

c. Fibrofatty proliferation

Increased mesenteric fat causes displacement of mesenteric vessels or other viscera. It is a specific sign of CD, representing long standing transmural inflammation.

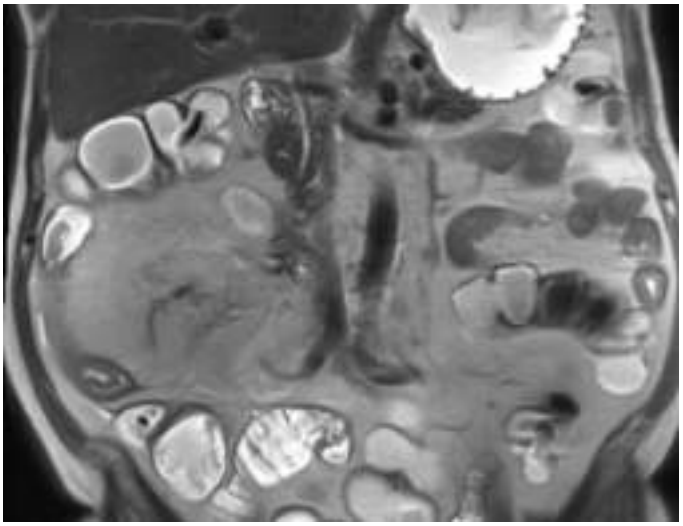

Fig 7 Fibrofatty proliferation in mesenetery

d. Lymph nodes

Hyper enhancement, enlargement and edema of lymph nodes adjacent to bowel seen on fat-saturated HASTE and True FISP images

e. Fistulas and sinuses

Seen as high signal intensity tracts on T2- weighted images or as enhancing tracts on post contrast enhanced T1 weighted sequences e.g. enterocolic, enteroenteric or enterocutaneous.

f. Abscess

As well defined, encapsulated collection of pus with high signal intensity on T2 – weighted and low signal intensity on T1 – weighted images typically with an enhancing rim.

CDAI CLINICAL SCORING OF DISEASE ACTIVITY

The index ranges from 0-600 and the cut off between remission and active disease originally taken to be 150 while values above 450 indicating active and very severe disease. In later work 150 -219 was defined as mildly active and 220-450 as moderately active disease.

Table 4 Crohn's Disease Activity Index (CDAI)

Variable Quantity	Multiple
Total Number of liquid or soft stools per day	2
Abdominal pain (0=none, 1=mild, 2=moderate, 3=severe)	5
General well being (0=well, 1=slightly under par, 2=poor, 3=very poor, 4=terrible)	7
Number of complications: arthralgias, iritis, erythema nodosum, pyoderma gangrenosa, aphthous ulcerations, anal fissure, anal fistula, anal abscess, fever >371 past week, intestinal obstruction	20
Opiates for diarrhea (no=0, yes=1,)	30
Abdominal mass (no=0, questionable=2, yes=5)	10
Deviation from normal hematocrit (N=42 for female, 47 for male)	6
% deviation from standard weight	1
Total CDAI	

COLONOSCOPIC REFERENCE

Endoscopic Crohn's disease index (SES-CD)

SES-CD is based of four endoscopic variables (ulcer size, ulcerated and affected surface, stenosis) scoring 0-3 in five ileocolonic segments.

SES-CD: sum of all variable – 1.4 x (number of affected segments)

Data has shown the score is reproducible but shows weak correlation to clinical indices (SES-CD to CDAI r = 0.371 and SES –CD to CRP r = 0.453), likely due to its inability to account for systemic or fistulating disease and involvement of proximal segments not visualized at CC.

It is simple and faster to calculate as compare to CDEIS but again use is limited in everyday endoscopic assessment (8).

Table 5 : SES- CD variables

Variables	0	1	2	3
Presence of ulcers	None	Aphthous ulcers (0.1-0.5 cm)	Large ulcers (0.5-2 cm)	Very larger ulcers (>2cm)
Ulcerated surface	None	<10%	10-30%	>30%
Affected surface	Unaffected segment	<50%	50-75%	>75%
Presence of narrowing	None	Single, can bepassed	Multiple, can be passed	Cannot be passed
Number of affected segments	All variables =0	At least one variable ≥ 1		

Table 6 SES scoring

	Ileum	Right colon	Transverse colon	Left colon	Rectum	SUM
Presence and size of ulcers						+
Extent of ulcerated surface						+
Extent of affected surface						+
Presence and type of narrowing						=
Sum of all variables						TOT
Affected segments	☐	☐	☐	☐	☐	

TOT – 1.4 × (number of affected segments) = SES-CD

STUDY DESIGN

This is a longitudinal prospective study.

STATISTICAL ANALYSIS:

The study attempted to test MRI MEGS score and DWI grade of disease activity against endoscopic and histological standard of reference on a per patient and per segment basis.

Data was described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Because the segmental ileal scores were interpreted as continuous variables, the spearman correlation was used to correlate the segmental ileal SES-CD score to the segmental ileal MEGS scoring. However since the DWI grades are non continuous variables, Chi square method was used to correlate them with MRI segmental MEGS score and endoscopic ileal segmental SES-CD score. Sensitivity, specificity, positive and negative predictive values and accuracy of each MR parameter and combined MRI score against colonoscopic reference were also calculated.

A probability value (*p*-value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

1. DEMOGRAPHIC AND CLINICAL DATA

A AGE DISTRIBUTION OF PATIENTS

The study was conducted on 32 patients diagnosed as Crohn' disease based on combination of endoscopic, histological, radiological and /or biochemical investigations. The age range of patients was 17-77 years with mean age of 43.8 years. Maximum patients in our study (n=17, 53.1%) were more than 40 years of age.

Table 7 Age distribution of patients

Age group	No. of cases	Percentage
< 30	9	28.1%
31-40	6	18.8%
> 40	17	53.1%
Total	32	100.0%

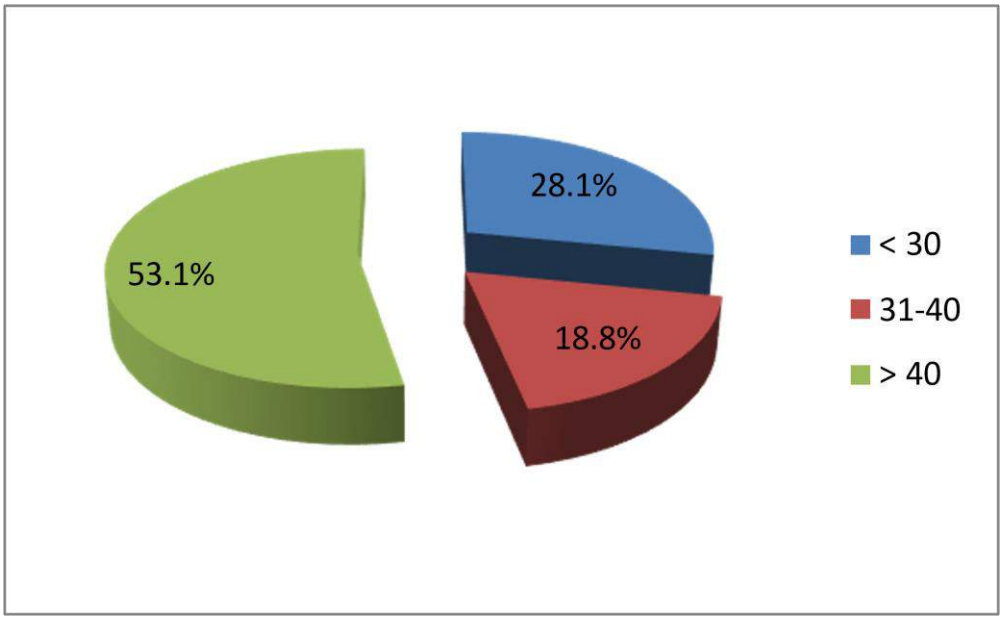

Figure 8 Age distribution of patients

B CROHN'S DISEASE ACITIVITY INDEX (CDAI)

The range for clinical CDAI scoring is from 111 to 699 in 32 patients with mean of 273. Most of the patients (n=18, 56.3 %) presented with moderate severity in CDAI 221-450 group.

TABLE 8 Distribution of patients according to clinical scoring of disease activity

CDAI GROUP		No. of cases	Percentage
< 150	Remission	8	25.0%
150-220	Mild	3	9.4%
221-450	Moderate	18	56.3%
451-1100	Severe	3	9.4%
Total		32	100.0%

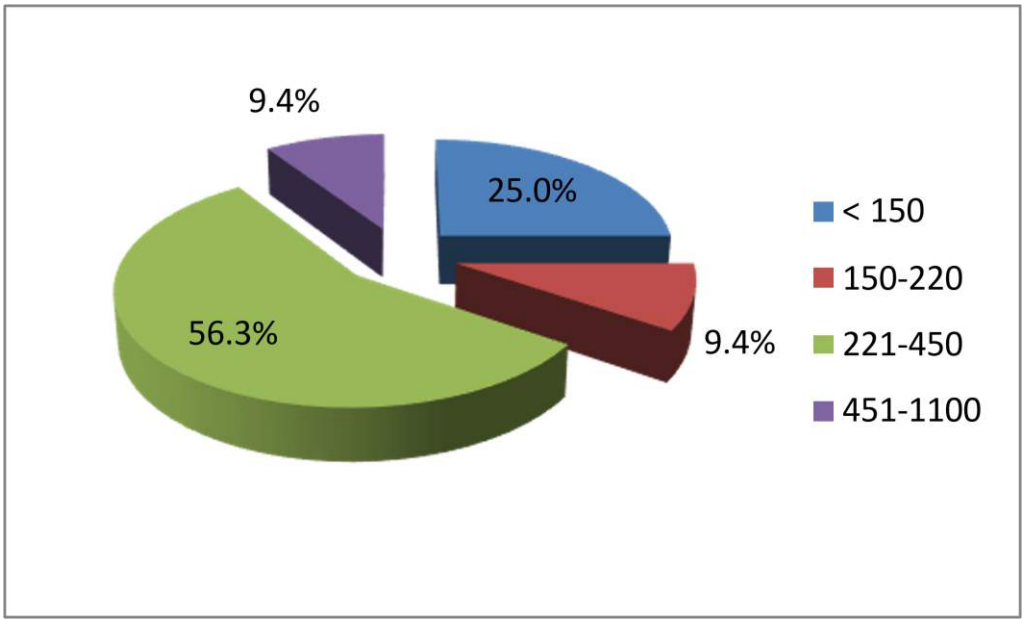

FIGURE 9 Distribution of patients according to clinical scoring of disease activity

2. ENDOSCOPIC DISEASE SEVERITY

The range for simple endoscopic score (SES- CD) was 2-15 with mean of 7.2 and standard deviation of 3.1. Maximum patients in our study (n=22, 68.8%) showed moderate disease activity.

TABLE 9 Distribution of patients according to endoscopic scoring of disease activity

SES CD GROUP		No. of cases	Percentage
2-6.0	Mild	10	31.3%
7-15.0	Moderate	22	68.8%
> 16	Severe	0	0.0%
Total		32	100.0%

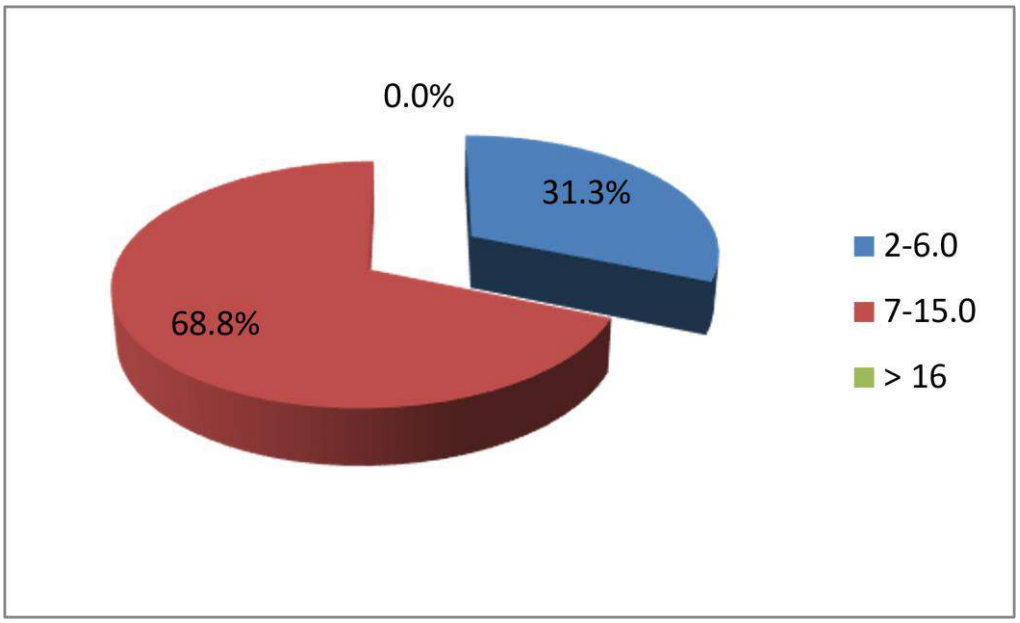

FIGURE 10 Distribution of patients according to endoscopic scoring of disease activity

3. MRI FINDINGS

A MRI EXTENT OF DISEASE

a. Disease distribution

The disease distribution was seen in different segments of gastrointestinal tract in addition to ileal disease documented on coloscopy

TABLE 10 Distribution of disease in various segments of gastrointestinal tract

SEGMENT	No. of cases	Percentage
Stomach	0	0.0%
Duodenum	0	0.0%
Jejunum	3	9.4%
Ileum	32	100.0%
Ileocecal valve	22	68.8%
Cecum	8	25.0%
Appendix	4	12.5%
Ascending Colon	1	3.1%
Transverse Colon	1	3.1%
Descending Colon	0	0.0%
Sigmoid	1	3.1%
Rectum	0	0.0%
Anal Canal	2	6.3%
Perianal Fistulae	6	18.8%

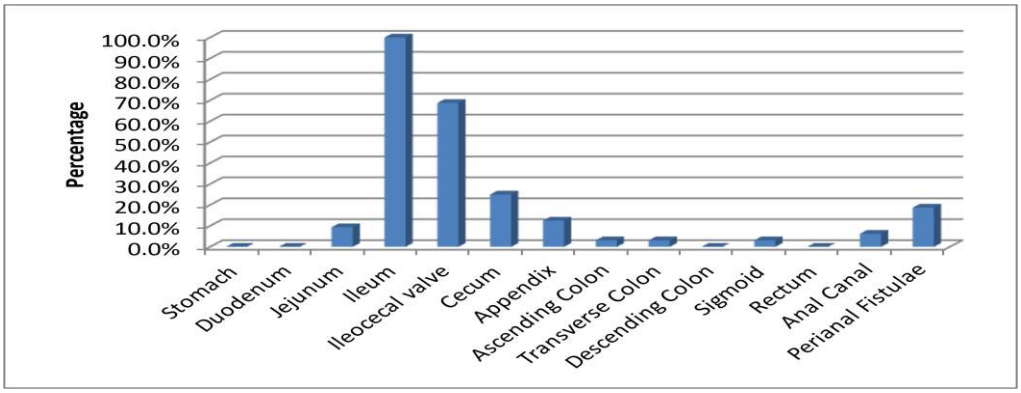

FIGURE 11 Distribution of disease in various segments of gastrointestinal tract

b. Number of segments involved

12 patients out of 32 had additional involvement of gastrointestinal segment in addition to ileal disease

TABLE 11 Number of segments involved

NO OF SEGMENTS	No. of cases	Percentage
1	20	62.5%
2	9	28.1%
3	2	6.3%
4	1	3.1%
Total	32	100.0%

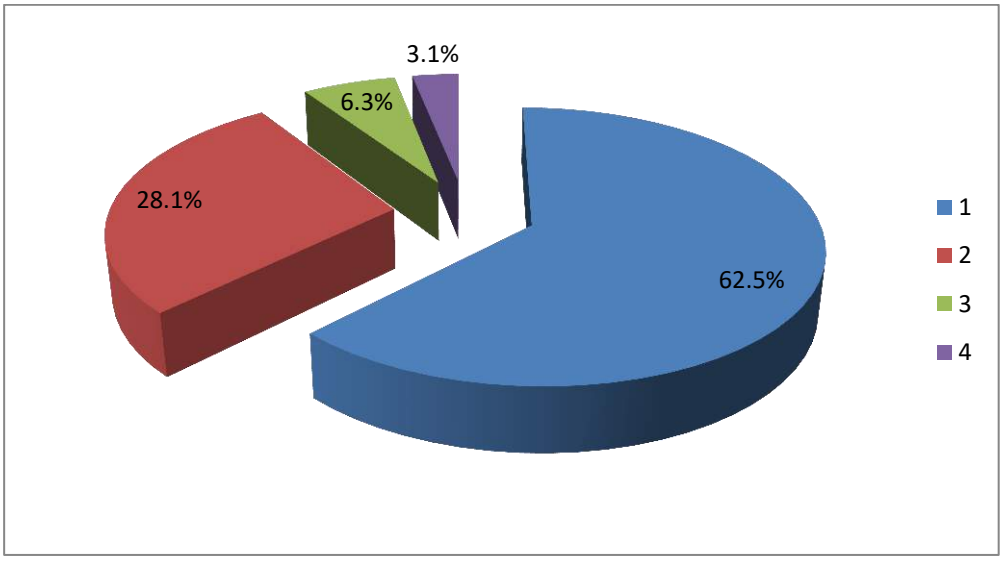

FIGURE 12 Number of segments involved

c. Length of segment involved

Most of the patients (n=20, 62.5%) had long segment involvement.

TABLE 12 Length of segment involved

Length of bowel involvement	No. of cases	Percentage
< 5cm	6	18.8%
5-15cm	6	18.8%
> 15 cm	20	62.5%
Total	32	100.0%

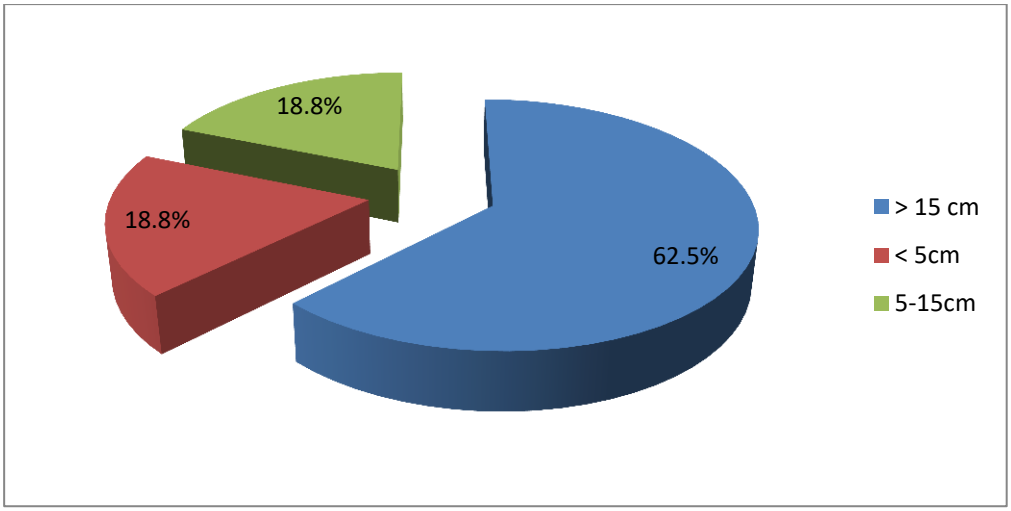

FIGURE 13 Length of segment involved

d. Skip segment involvement

N=20 , 62.5% patients had skip segments involvement

TABLE 13 Skip segment involvement

Skip Segments	No. of cases	Percentage
No	12	37.5%
Yes	20	62.5%
Total	32	100.0%

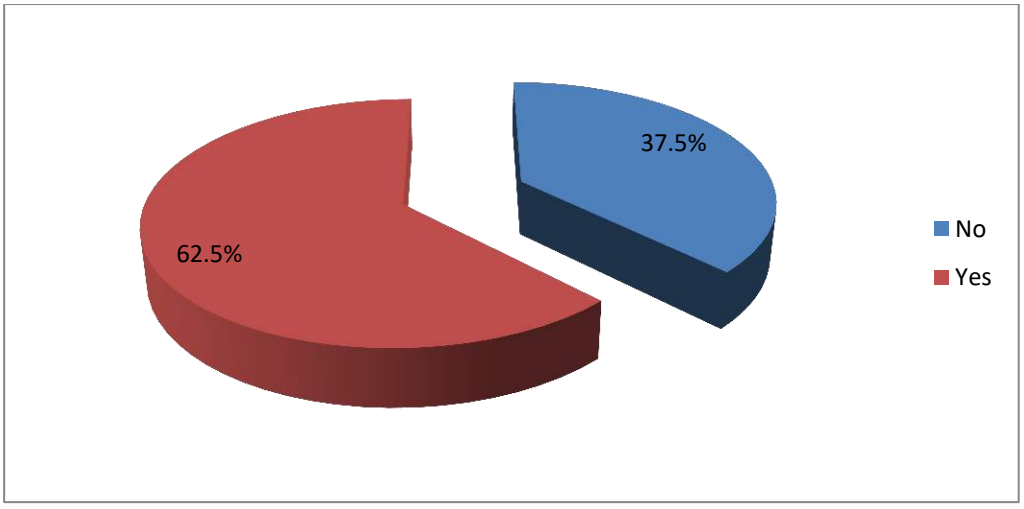

FIGURE 14 Skip segment involvement

B DISEASE APPEARANCE ON MRI

1 Mural features

a. Mural T2 signal intensity

In 43.8 % (n=29) cases, diseased bowel wall was of intermediate signal intensity on T2WI, while dark and hyperintense signal was seen in 21.9% (n=7) and 34.4% (n=11) cases respectively

TABLE 14 Mural T2 signal intensity

T2 signal	No. of cases	Percentage
Dark	7	21.9%
Intermediate	14	43.8%
Hyperintense	11	34.4%
Total	32	100.0%

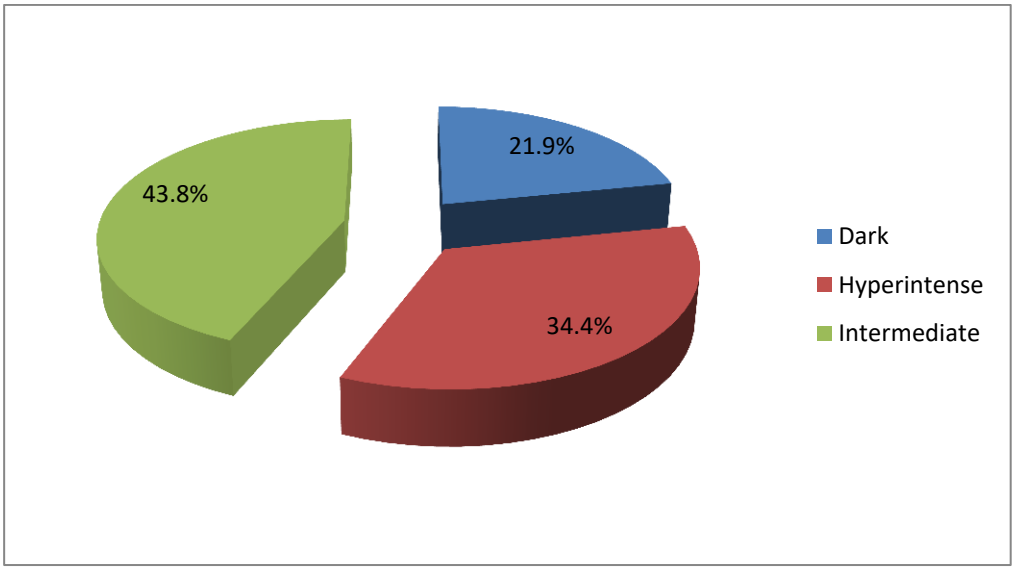

FIGURE 15 Mural T2 signal intensity

b. Wall thickness

It was measured on T2 images in millimetres. More the wall thickness, more is the severity score.

TABLE 15 Wall thickness on T2 weighted images

Wall thickness	No. of cases	Percentage
3-5.0	9	28.1%
5-7.0	10	31.3%
> 7	13	40.6%

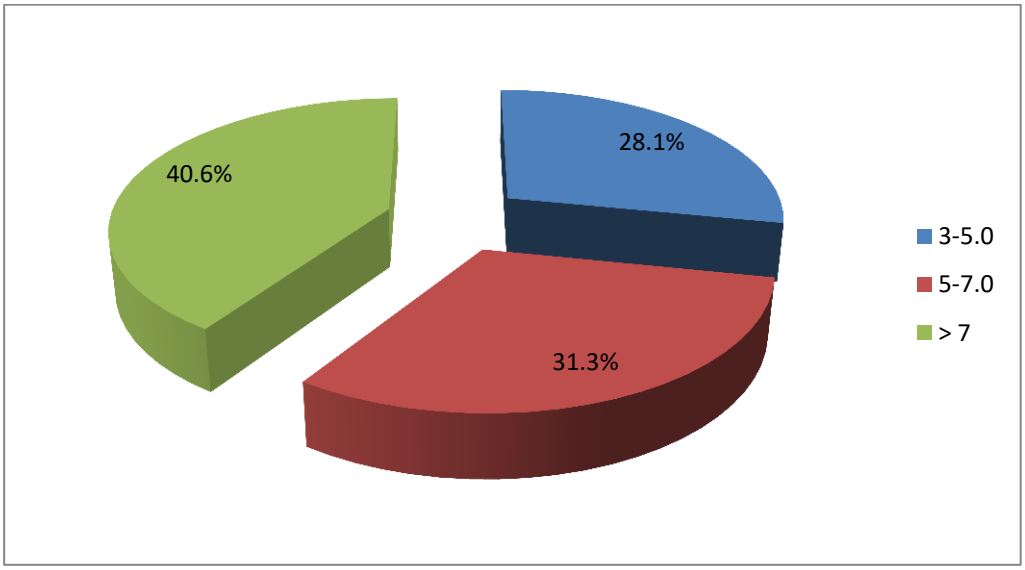

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FIGURE 16 Wall thickness on T2 weighted images

c. Intensity of mural contrast enhancement

On contrast enhanced images, intensity of wall enhancement was compared to the vessel with grade 3 equivalent to vessel signal intensity on T2 fat sat images.

TABLE 16 Intensity of mural contrast enhancement

Wall enhancement	No. of cases	Percentage
grade1	8	25.0%
grade2	12	37.5%
grade3	12	37.5%
Total	32	100.0%

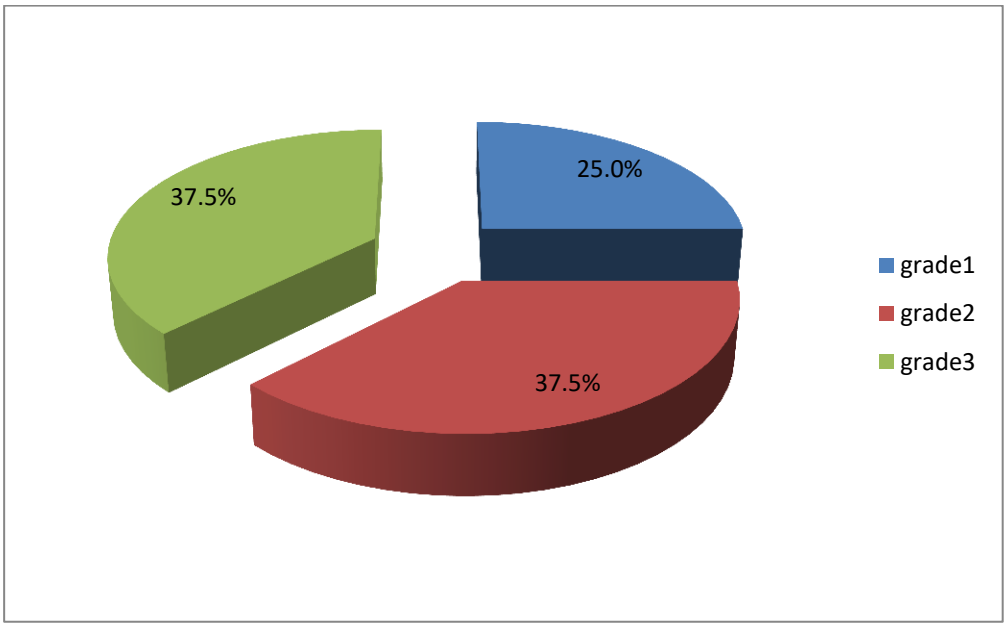

FIGURE 17 Intensity of mural contrast enhancement

d. Mural enhancement pattern

Stratified or layered pattern is due to bright inflamed mucosa and hypoenhancing edematous submucosa.

Diffuse homogenous pattern is due to homogenous enhancement of entire wall thickness due to transmural inflammation.

Mural stratified pattern was seen in 59.4% cases (n= 19).

TABLE 17 Mural enhancement pattern

Enhancement Pattern	No. of cases	Percentage
homogenous	13	40.6%
Mural, stratified	19	59.4%
Total	32	100.0%

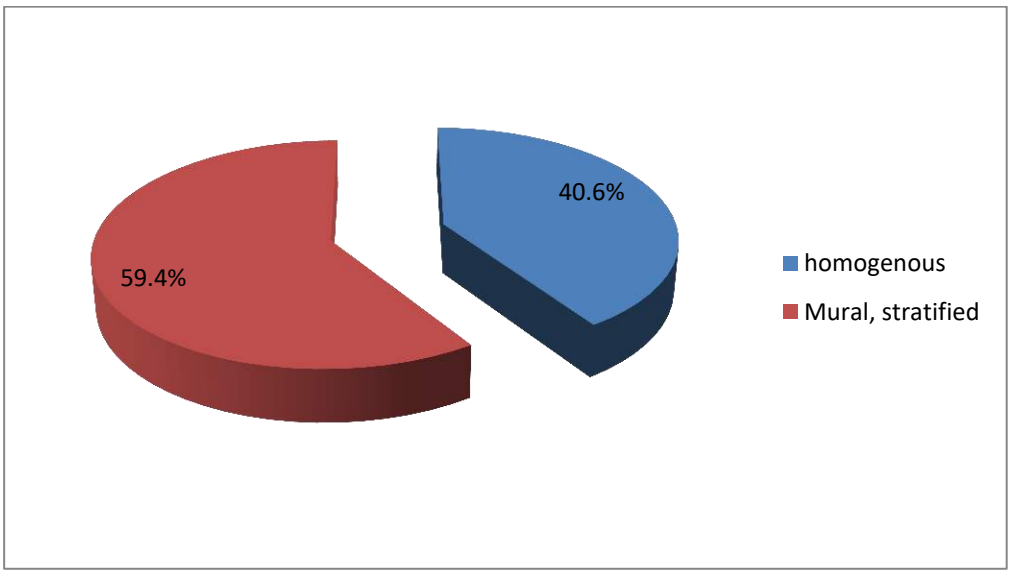

FIGURE 18 Mural enhancement pattern

2 Extramural features

a. Comb sign

Comb sign depicts increased mesenteric vascularity during active disease. It was positive in 26 % of cases (n= 26).

TABLE 18 Comb sign on MRI

Comb's Sign	No. of cases	Percentage
NO	6	18.8%
YES	26	81.3%
Total	32	100.0%

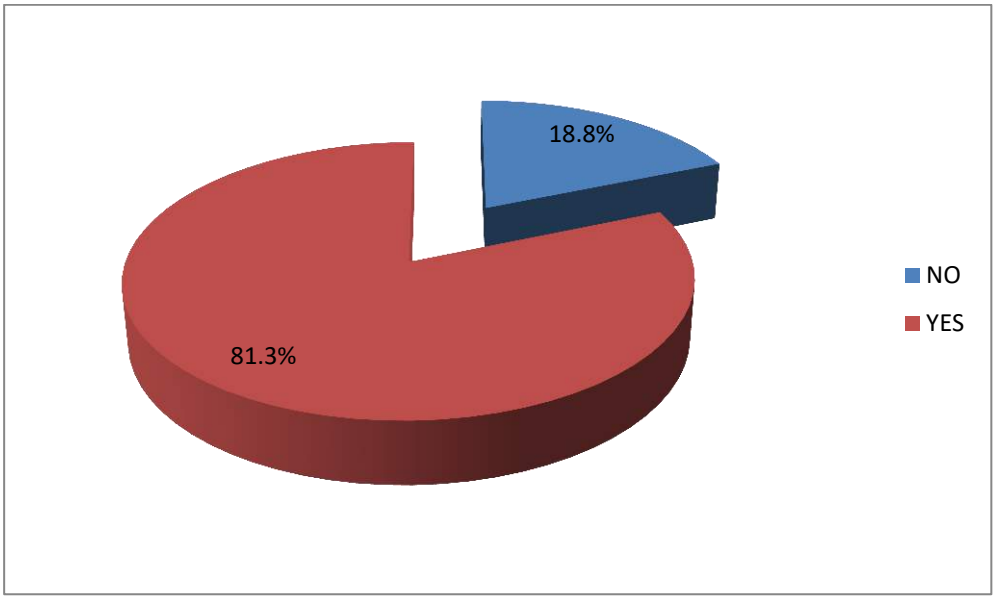

FIGURE 19 Comb sign on MRI

b. Fibrofatty proliferation

It is a specific sign of crohn's disease representing active/chronic transmural inflammation. It is positive in 65.6 % of cases (n= 21)

TABLE 19 Fibrofatty proliferation on MRI

Fibrofatty proliferation	No. of cases	Percentage
NO	11	34.4%
YES	21	65.6%
Total	32	100.0%

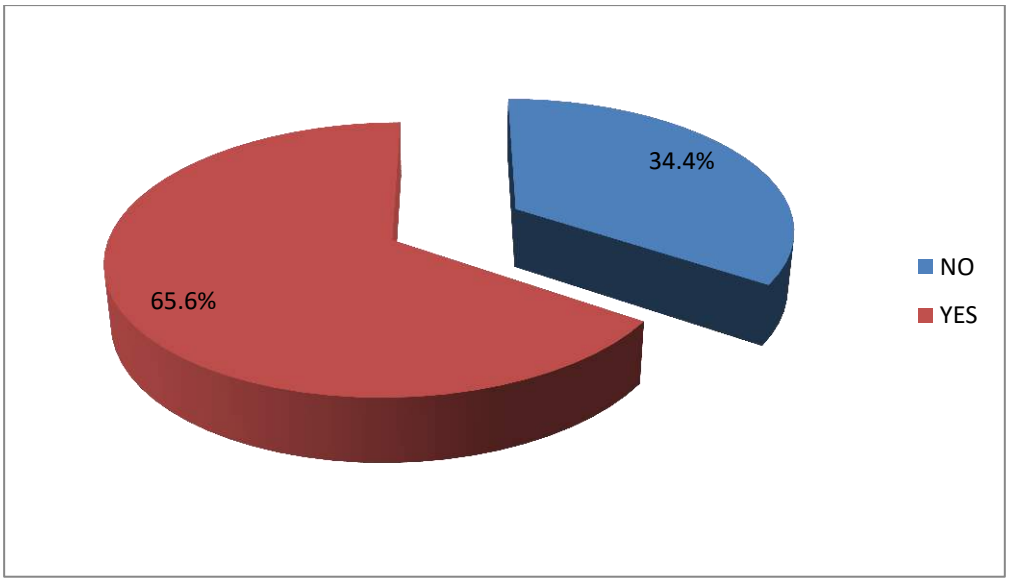

FIGURE 20 Fibrofatty proliferation on MRI

c. Perienteric changes

Increased mesenteric signal is best seen on fat saturated T2 weighted images.

TABLE 20 Perienteric changes on T2 fat saturated images

Perienteric changes	No. of cases	Percentage
NO	20	62.5%
YES	12	37.5%
Total	32	100.0%

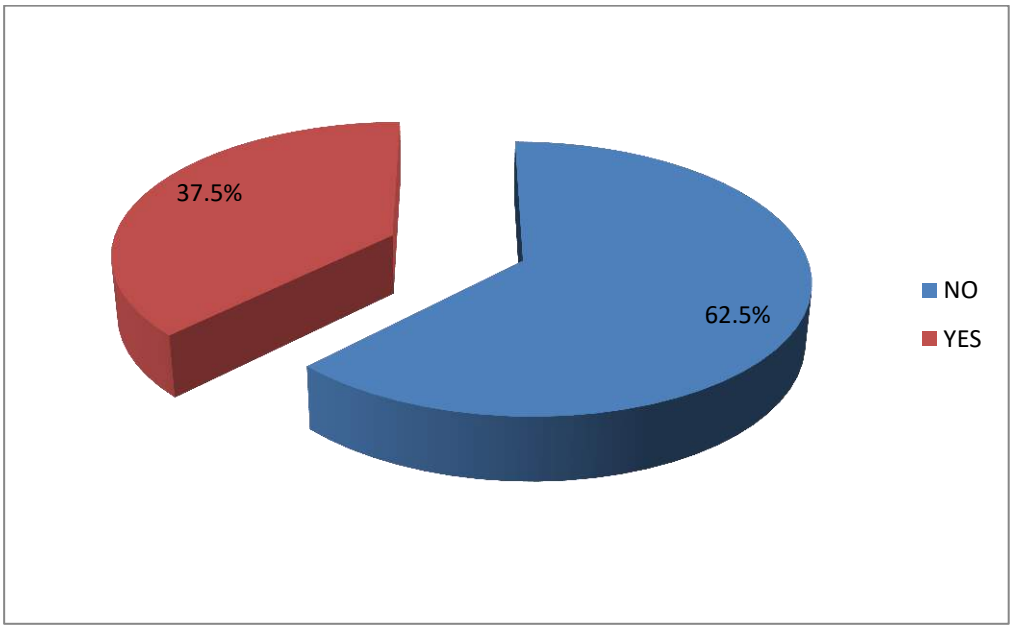

FIGURE 21 Perienteric changes on T2 fat saturated images

d. Fistula / sinus

These were seen as high signal intensity tracts on T2 weighted images or as enhancing tracts on post contrast images. These were seen in 18.8% cases (n=6).

TABLE 21 Associated Fistula/sinus on MRI

Fistulae/ Sinus	No. of cases	Percentage
NO	26	81.3%
YES	6	18.8%
Total	32	100.0%

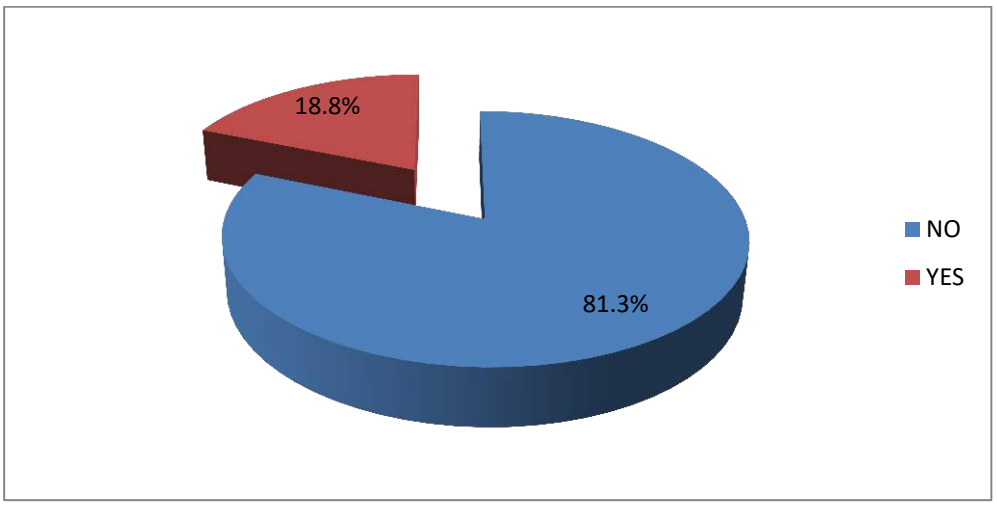

FIGURE 22 Associated Fistula/sinus on MRI

e. Reduced pliability

Pliability was reduced in 87.5% cases (n=28).

TABLE 22 Reduced pliability on CINE images

Pliability	No. of cases	Percentage
Preserved	4	12.5%
Reduced	28	87.5%
Total	32	100.0%

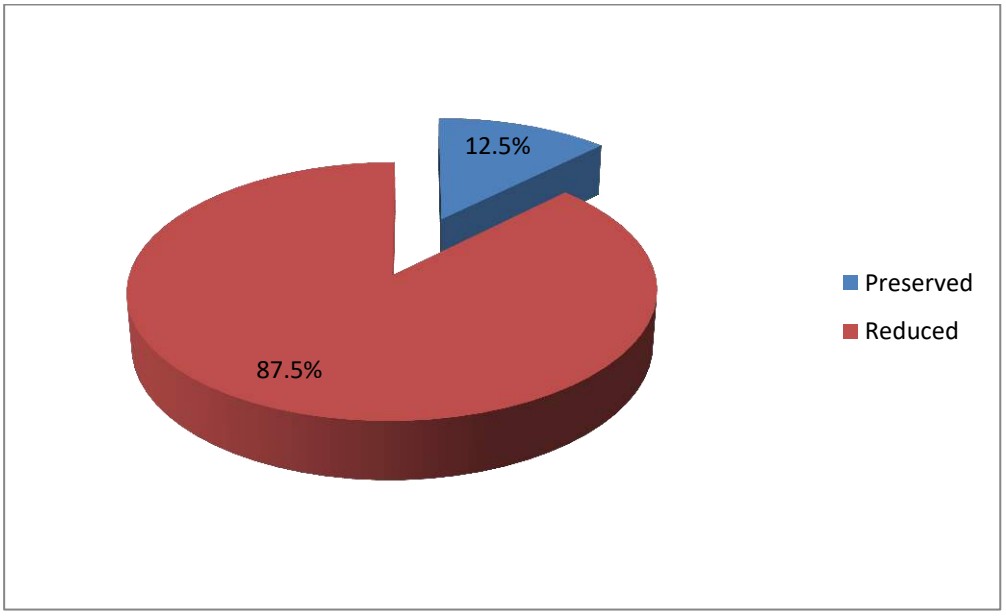

FIGURE 23 Reduced pliability on CINE images

f. Lymphadenopathy

Hyperenhancement or enlargement of the lymph nodes adjacent to the bowel seen on fat saturated HASTE and TrueFISP images. Lymphadenopathy was seen in 50% cases (n=16).

TABLE 23 Associated Lymphadenopathy on MRI

Lymphadenopathy	No. of cases	Percentage
Absent	16	50.0%
Present	16	50.0%
Total	32	100.0%

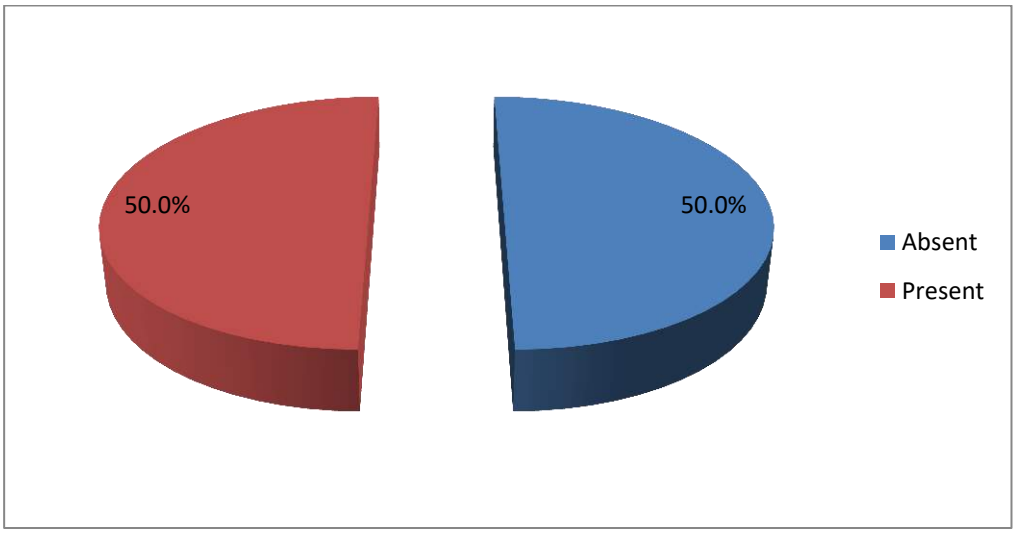

FIGURE 24 Associated Lymphadenopathy on MRI

g. Obstruction

Obstruction as a complication was seen in 9.4% cases (n=3)

TABLE 24 Associated Obstruction on MRI

Obstruction	No. of cases	Percentage
NO	29	90.6%
YES	3	9.4%
Total	32	100.0%

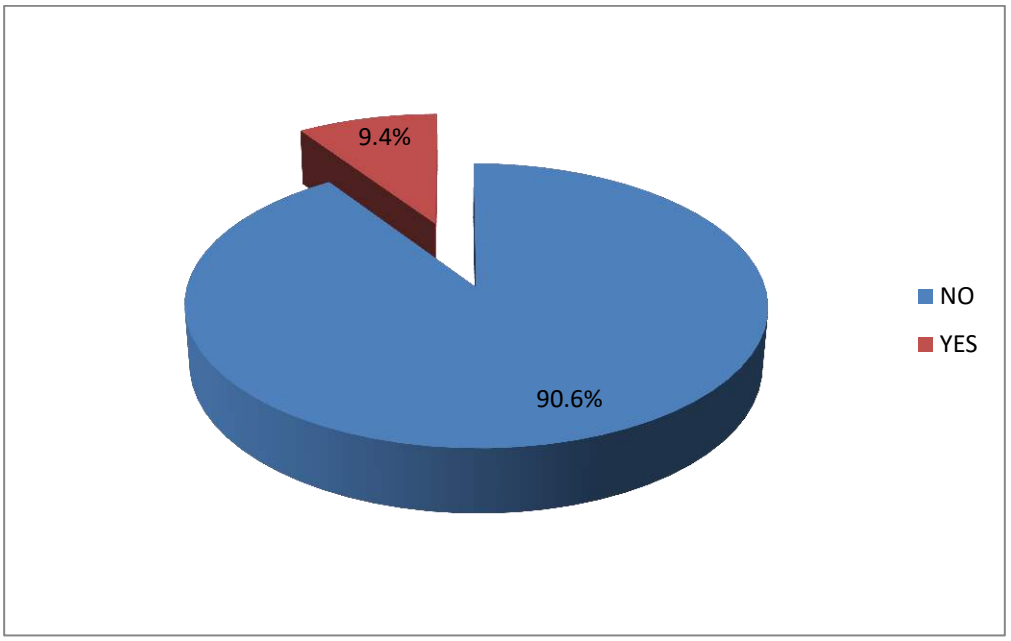

FIGURE 25 Associated Obstruction on MRI

C DISEASE ACTIVITY SCORING ON MRI

Disease activity scoring has been done using ileal MRI enterography global score (MEGS) and compared against colonoscopic reference.

TABLE 25 Distribution of patients according to MRI scoring of disease activity

SEGMENTAL MEGS group	No. of cases	Percentage
Mild	16	50.0%
Moderate	11	34.4%
Severe	5	15.6%
Total	32	100.0%

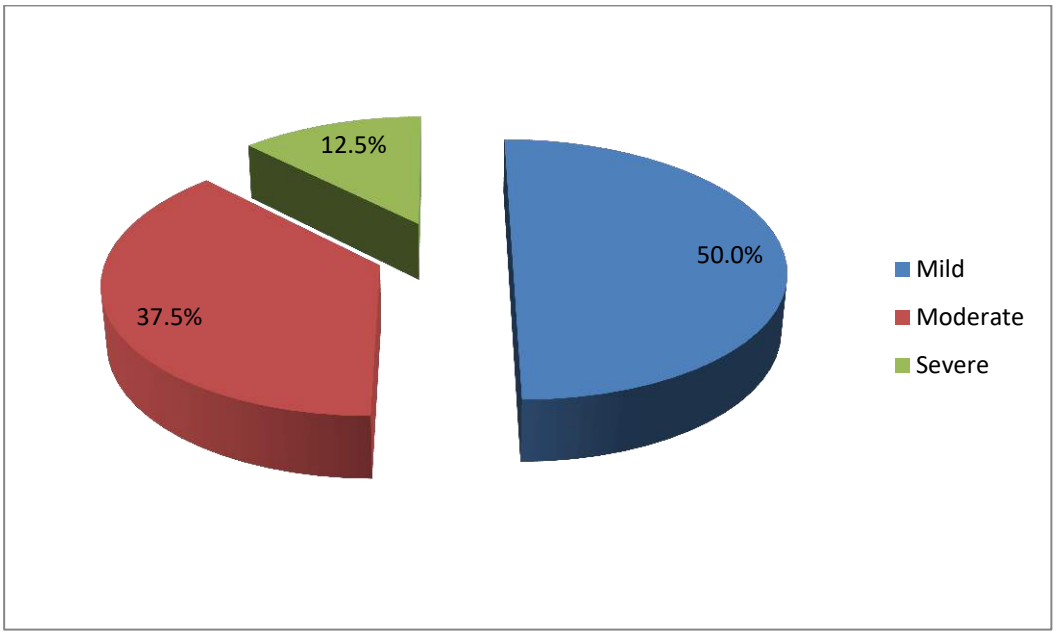

FIGURE 26 Distribution of patients according to MRI scoring of disease activity

The range for MEGS score was 2-30 with mean of 15.4.

Most of the patients had mild disease severity (n= 16, 50%) with MEGS ranging between 5-15

4.CLINICAL SCORING AS MARKER FOR DISEASE ACTIVITY A ENDOSCOPIC REFERENCE

The correlation between clinical CDAI scoring and endoscopic SES-CD scoring for disease activity was very weak and not statistically significant with pearsman correlation coefficient of .313

Table 26 Correlation between CDAI with endoscopic scores

	Spearman's rho	SES CD
CDAI	Correlation Coefficient	0.313
	p-value	0.082
	N	32

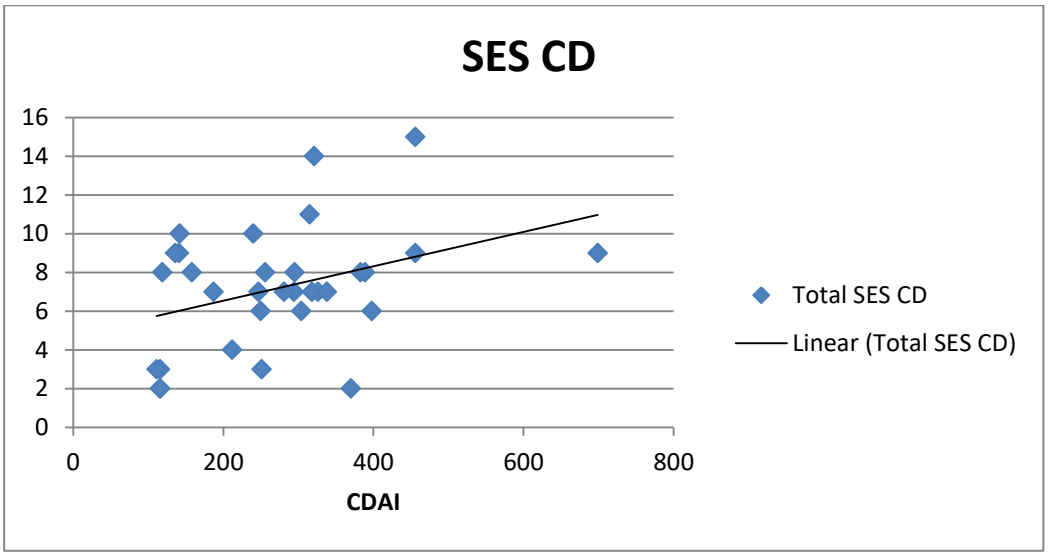

FIGURE 27 scattered graph between CDAI and total simple endoscopic score

B RADIOLOGICAL REFERENCE

The correlation between clinical CDAI scoring and MRI MEGS scoring for disease activity was very weak and not statistically significant

Table 27 Correlation between CDAI with MRI MEGS score

	Spearman's rho	SEGMENTAL MEGS MRI SCORING
CDAI	Correlation Coefficient	0.004
	p-value	0.985
	N	32

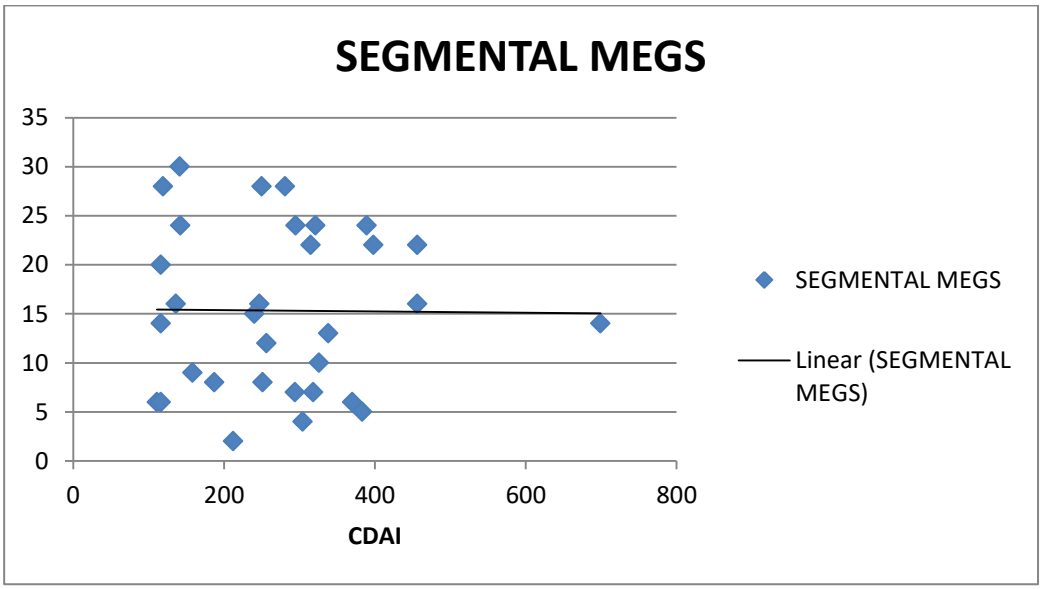

FIGURE 28 scattered graph between CDAI and MRI score for disease activity

5. MRI PARAMETERS AND MEGS SCORING AS MARKER FOR DISEASE ACITIVITY WITH ENDOSCOPIC REFERENCE

j. MEGS SCORE AS MARKER FOR DISEASE ACTIVITY WITH ENDOSCOPIC REFERENCE

The correlation between endoscopic SES-CD scoring and MRI MEGS scoring for disease activity was statistically significant (p value 0.007)

Table 28 Correlation between endoscopic SES-CD scoring and MRI MEGS scoring for disease activity

	Spearman's rho	SEGMENTAL MEGS
Ileal SES CD	Correlation Coefficient	0.471
	p-value	0.007
	N	32

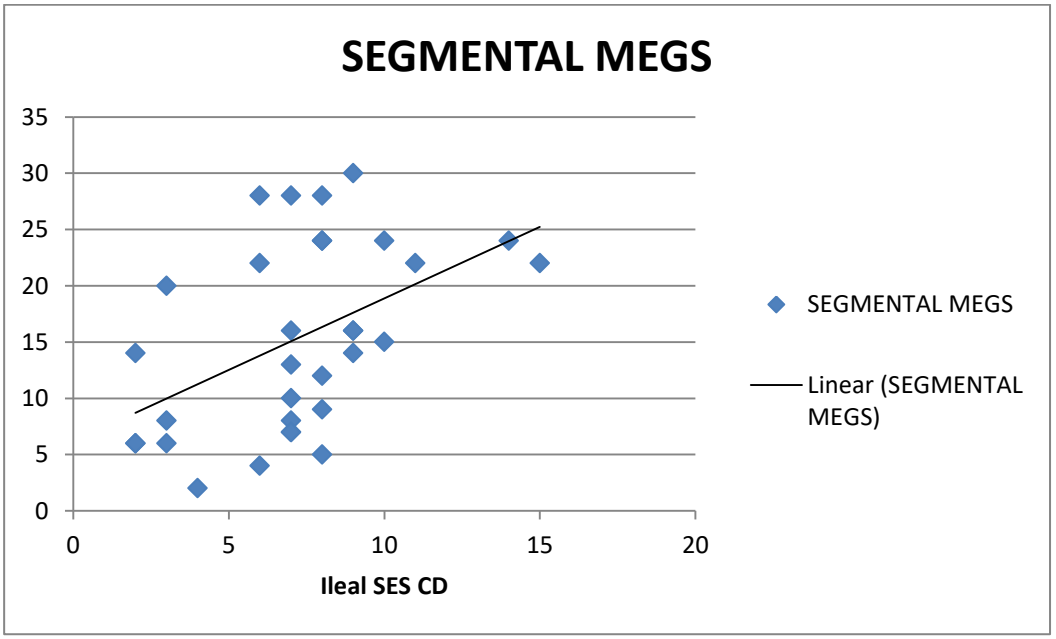

FIGURE 29 Scattered graph between endoscopic SES-CD scoring and MRI MEGS scoring for disease activity

In our patient cohort, MRE demonstrated a sensitivity of 92 % and a specificity of 57.4 % compared to colonoscopy. Considering active disease on colonoscopy with SES -CD more than 5 and MRI MEGS score more than 6.

TABLE 29 Statistical values for MRI scoring in assessment of disease activity with endoscopic reference

		SES CD GROUP		
		<_5	> 5	Total
MEGS	<_6	4	2	6
	>6	3	23	26
Total		7	24	32

Statistic	**Value**	95% CI
Sensitivity	**92.00%**	54.63% to 92.18%
Specificity	**57.14%**	26.24% to 87.84%
Positive Predictive Value (*)	**88.46%**	65.81% to 90.37%
Negative Predictive Value (*)	**66.67%**	32.31% to 75.10%
Accuracy (*)	**84.38%**	53.25% to 86.25%

k. DWI GRADE AS MARKER FOR DISEASE ACITIVITY WITH ENDOSCOPIC REFERENCE

The correlation between endoscopic SES-CD scoring and DWI grading for disease activity was statistically significant (p value 0.03)

Table 30 Correlation between endoscopic SES-CD scoring and DWI grading for disease activity

		SES CD GROUP				Total	Chi-square value	p-value
		2-6	2-6	7-15	7-15			
Ileal DWI grade	1	4	40.0%	1	4.5%	5	6.998	0.030
	2	2	20.0%	4	18.2%	6		
	3	4	40.0%	17	77.3%	21		

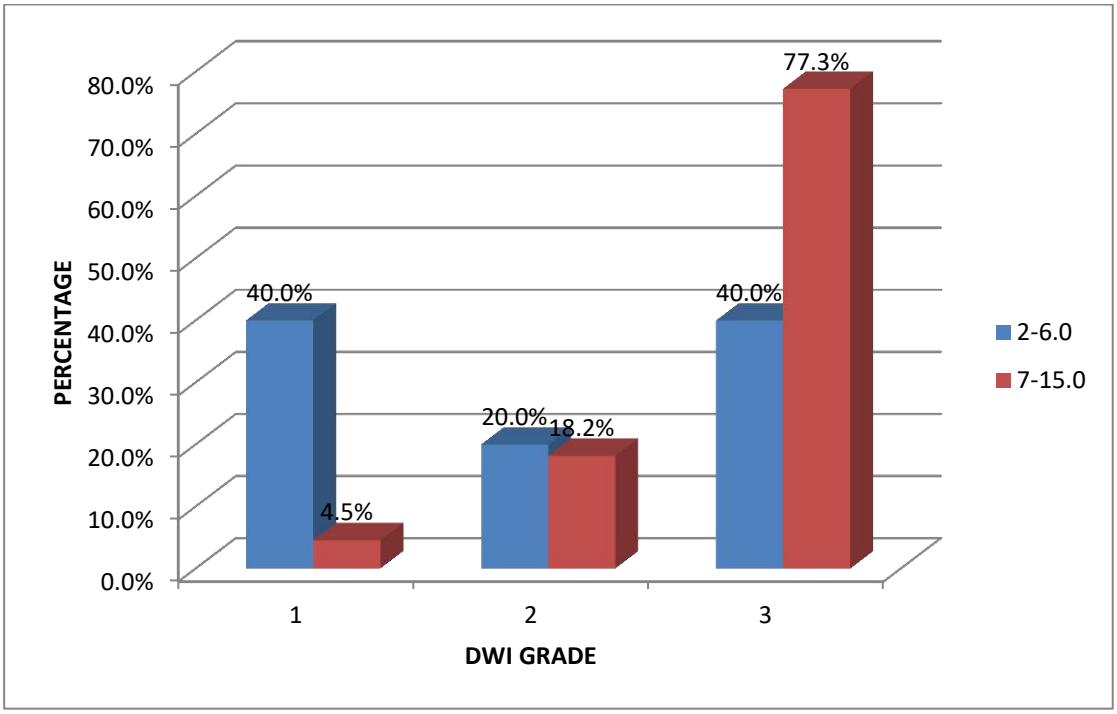

Figure 30 Correlation between endoscopic SES-CD scoring and DWI grading for disease activity

In our patient cohort, DWI demonstrated a sensitivity of 92 % and a specificity of 42.8 % compared to colonoscopy. Considering active disease on colonoscopy with SES -CD more than 5 and DWI score more than 1

TABLE 31 Statistical values for DWI grading in assessment of disease activity with endoscopic reference

		SES CD GROUP		
		<_5	> 5	Total
DWI SCORE ileal	1	3	2	5
	2-3.0	4	23	27
Total		7	25	32

Statistic	**Value**	95% CI
Sensitivity	**92.00%**	77.16% to 99.88%
Specificity	**42.86%**	12.16% to 73.76%
Positive Predictive Value (*)	**85.19%**	67.67% to 85.41%
Negative Predictive Value (*)	**60.00%**	33.77% to 96.91%
Accuracy (*)	**81.25%**	60.03% to 90.72%

I. INDIVIDUAL MRI PARAMETERES AS MARKER FOR DISEASE ACITIVITY WITH ENDOSCOPIC REFERNECE

The correlation between endoscopic SES-CD scoring and individual MRI parameters for disease activity is as follows-

Table 32 Correlation between endoscopic SES-CD scoring and individual MRI parameters for disease activity

		SES CD GROUP				Total	Chi-square value	p-value
		2-6.0	2-6.0	7-15.0	7-15.0			
Length of bowel involvement	< 5cm	2	20.0%	4	18.2%	6	0.039	0.981
	5-15cm	2	20.0%	4	18.2%	6		
	>15 cm	6	60.0%	14	63.6%	20		
T2 signal	dark	4	40.0%	3	13.6%	7	3.106	0.212
	Intermediate	4	40.0%	10	45.5%	14		
	Hyperintense	2	20.0%	9	40.9%	11		
Wall thickness	3-5mm	6	60.0%	3	13.6%	9	7.367	**0.025**
	>5-7mm	2	20.0%	8	36.4%	10		
	>7mm	2	20.0%	11	50.0%	13		
Wall enhancement	grade1	4	40.0%	4	18.2%	8	1.745	0.418
	grade2	3	30.0%	9	40.9%	12		
	grade3	3	30.0%	9	40.9%	12		
Enhancement Pattern	homogenous	7	70.0%	6	27.3%	13	5.203	**0.049**
	Mural, stratified	3	30.0%	16	72.7%	19		

Ulcers	No	8	80.0%	14	63.6%	22	0.857	0.355
	Yes	2	20.0%	8	36.4%	10		
Comb's Sign	NO	1	10.0%	5	22.7%	6	0.731	0.393
	YES	9	90.0%	17	77.3%	26		
Fibrofatty proliferation	NO	2	20.0%	9	40.9%	11	1.332	0.248
	YES	8	80.0%	13	59.1%	21		
Perienteric changes	NO	9	90.0%	11	50.0%	20	4.693	**0.030**
	YES	1	10.0%	11	50.0%	12		
Fistulae/ Sinus	NO	10	100.0%	16	72.7%	26	3.357	0.067
	YES	0	0.0%	6	27.3%	6		
Pliability	Preserved	2	20.0%	2	9.1%	4	0.748	0.572
	Reduced	8	80.0%	20	90.9%	28		
Lymphadenopathy	Absent	5	50.0%	11	50.0%	16	0.000	1.000
	Present	5	50.0%	11	50.0%	16		
Obstruction	NO	9	90.0%	20	90.9%	29	0.007	0.935
	YES	1	10.0%	2	9.1%	3		
Total		10	100.0%	22	100.0%	32		

Statistically significant correlation was found for wall thickness, enhancement pattern and perienteric changes with endoscopic scoring for disease activity.

6. CORRELATION OF MRI MEGS SCORING AND DWI SCORING FOR DISEASE ACTIVITY

The correlation between DWI scoring and MRI MEGS scoring for disease activity was statistically significant (p value 0.002)

TABLE 33 Correlation between DWI scoring and MRI MEGS scoring for disease activity

		SEGMENTAL MEGS group						Total	Chi-square value	p-value
		5-15.0	5-15.0	15-25	15-25	25-34	25-34			
DWI SCORE ileal	1	5	31.3%	0	0.0%	0	0.0%	5	16.762	0.002
	2	6	37.5%	0	0.0%	0	0.0%	6		
	3	5	31.3%	11	100.0%	5	100.0%	21		

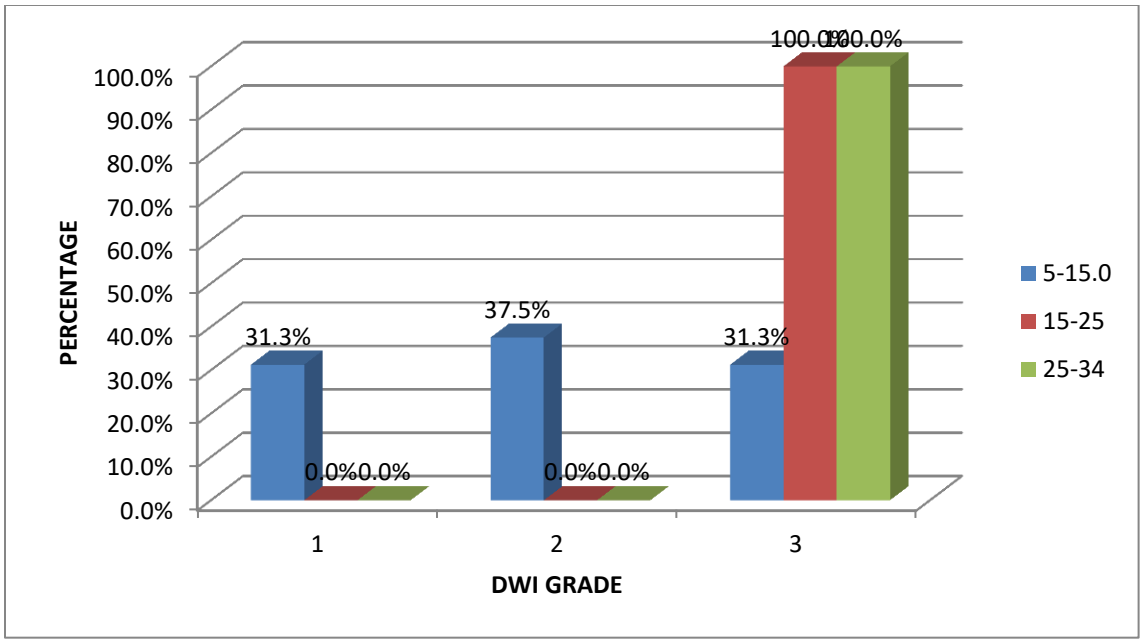

FIGURE 31 Correlation between DWI scoring and MRI MEGS scoring for disease activity

DISCUSSION

The total number of patients included in the study was 32 all having isolated ileal disease documented on colonoscopy. The results showed that based on the cohort distribution by age, Crohn's disease occurred more frequently in patients above 40 years of age with an average age of 43.8 years. Previous studies have suggested bimodal distribution [(1)] of incidence of Crohn's disease as a function of age. The disease tends to strike people in their teens and twenties and people in their fifties through seventies. It is rare in early childhood.

This study aimed to evaluate the correlation of clinical, colonoscopic, radiological and histological markers of disease activity. Although assessment of disease activity is vital in the management of Crohn's disease , there is no single accepted standard of reference. In this study, the qualitative ileal segmental MRI MEGS scoring and subjective grading of DWI signal were correlated with colonoscopic and histological references.

Based on the cohort distribution by CDAI scoring, most patients presented with moderate disease severity with a mean of 273. The correlation between clinical CDAI scoring and endoscopic SES-CD scoring for disease activity was very weak and not statistically significant with pearsman correlation coefficient of 0.313. The correlation between clinical CDAI scoring and MRI MEGS scoring for disease activity was also very weak and not statistically significant.

The CDAI has been used for decades to study the effectiveness of medical therapies for treating patients with CD. However it is a composite measure that includes patient's symptoms, hematocrit and physical examination findings. The CDAI has fallen out of favour for use in clinical trials due to weak correlation with objective measures of inflammation and endoscopically defined inflammation in particular. There are many possible explanations for the weak correlations observed between clinical symptoms and SES-CD. Pain is a complex phenomenon with many

potential causes, some of which will differ from those that cause diarrhea. Abdominal Pain in patients with CD can result from noninflammatory processes including irritable bowel syndrome, the effects of surgery on bowel motility, submucosal fibrosis, adhesions, and stricture formation, the latter being more relevant in the small intestines than in the colon. The transmural nature of CD could result in inflammation of enteric neurons in the absence of significant mucosal inflammation. Whether abdominal pain would correlate better with other measures of bowel damage, including cross-sectional imaging or biomarkers, needs to be determined.

Some CDAI items are only weakly linked to inflammation and/or are heavily influenced by other confounding variables. For example, although weight loss is a manifestation of uncontrolled inflammation in patients with active CD, treatment with corticosteroids may offset this effect without having a strong benefit on endoscopically defined disease activity. Likewise, hematocrit is affected by blood volume status, blood loss from causes other than CD such as menstruation, and bone marrow suppression from immunosuppressive drugs. The original selection of the CDAI items was based upon regression of items generated by clinicians with physician assessment of clinical disease activity as a gold standard, as opposed to endoscopic assessment of bowel inflammation. However, it must be acknowledged that in previous studies, the correlation with endoscopic findings with CDAI was qualitatively stronger in those patients with colonic disease. The stronger correlation in those with colonic disease may reflect the colon’s role in water absorption or merely the greater extent of mucosal involvement due to the relative size of the colon compared with the ileum. Alternatively, there is a smaller range of SES-CD values for isolated ileal disease, which could limit the strength of the correlation. Finally, only a limited portion of the ileum is visualized during colonoscopy, and as such there is a greater risk of misclassification of disease activity in the ileum.

Regarding the disease extent on MRI, out of all patients with isolated ileal

disease on colonoscopy, most patients (62%) in our study had long and skip segment involvement on MRI with additional involvement of jejunum, colon and appendix in few patients. MRI also demonstrated extraintestinal manifestations like perienteric changes in 62.5 %, comb's sign in 81.2 %, fibrofatty proliferation in 65.6%, fistula/ sinus in 18.8%, lymphadenopathy in 50% and obstruction in 9.4% cases. According to a study [68], Adding MRI to the information from colonoscopy changed the clinicians' confidence grade in a higher proportion of patients than adding colonoscopy to information from MRI for the diagnosis of disease activity (10 vs 4%, $p = 0.03$), stenosis (25 vs 9%, $p < 0.001$), fistula (31 vs 0%, $p < 0.001$) and internal abscess (27 vs 0%, $p < 0.001$). Pelvic MRI has become part of the standard imaging workup of patients with Crohn's disease and suspected perianal involvement [69]. The lifetime risk of perianal fistula formation in Crohn's disease ranges from 30–50%, with the presence of a fistula leading to significant morbidity due to cutaneous drainage or perianal abscess formation. The superior soft tissue contrast of MRI provides detailed anatomic delineation of the anal sphincter complex. It is important to determine the anatomic relationship of perianal fistulae with the internal and external anal sphincters, as well as the levator ani complex, as these can affect the surgical approach and closure technique [70]. Additionally, MRI is sensitive for detection of perianal abscesses requiring urgent intervention.

MR features of signs of active bowel inflammation in inflammatory bowel disease include bowel wall thickening, bowel wall hyperintensity and hyper-enhancement. A layered pattern of bowel wall enhancement consisting of brightly enhancing mucosa (from inflammation) and hypoenhancing submucosa (from edema) has also been shown to be a specific sign of active bowel inflammation [56]. An advantage of MRI over ileocolonoscopic evaluation of IBD is its ability to detect associated mesenteric inflammatory changes suggestive of active disease.

Mesenteric features associated with IBD include lymphadenopathy, vasa recta hypervascularity, and fibrofatty infiltration.

MRI evaluation of the bowel relies predominantly on three sequences [71]. The first is a single shot fast spin echo T2 sequence with half-Fourier reconstruction (e.g. HASTE, SSFSE) that provides motion-free T2 weighted images for evaluating for bowel wall edema and extraluminal fluid collections. The second is balanced steady state free precession (e.g. True FISP, FIESTA) which is exquisitely sensitive to mesenteric changes such as hypervascularity, fibrofatty proliferation, and fistulae. The third is a dynamic fast 3D spoiled gradient echo T1 fat-suppressed post-contrast sequence (e.g. VIBE, LAVA) to evaluate the pattern of bowel enhancement. Other technological innovations leading to effective MR bowel imaging include higher magnetic field strengths (1.5 T and more recently 3 T), multichannel phased array coils, and parallel image processing. These technological advances have led to the development and clinical implementation of MRI protocols designed to evaluate the small bowel (MR enterography, enteroclysis) and colon (MR colonography).

MR enterography has emerged as a potentially useful investigation for assessment of Crohn's disease but there are inconsistencies in current literature regarding techniques, MRI parameters and reference standard applied (symptoms scoring, biochemical markers, endoscopic, histological and surgical). MRE is intuitively a very attractive proposition for management of CD but there is no robust reference standard to assess its diagnostic efficacy. The study attempted to test MRI MEGS score and DWI grade of disease activity against endoscopic standard of reference.

Most of the patients had mild disease severity (n= 16, 50%) with MEGS ranging between 5-15. The data in our study showed that ileal segmental MRI MEGS score of disease activity correlated significantly (r=0.47, p value 0.007) with simple endoscopic score (SES-CD) on a per patient and per segment basis, providing some validity to their use in clinical practice.

In our patient cohort, MRE demonstrated a sensitivity of 92 % and a specificity of 57.4 % with accuracy of 84.3% compared to colonoscopy, considering active disease on colonoscopy with SES -CD more than 5 and MRI MEGS score more than 6. Rimola et al. [67] proposed and validated a simplified Magnetic Resonance Index activity score that appeared to be a very good tool for assessing the disease activity, permitting a proper patient classification into three groups: inactive, mild, moderate to severe in ways that closely mimic the endoscopic score.

Our results compare favorably with the results of previous, smaller studies. In a study of 31 patients, Lee et al. reported the sensitivity of MRE as 83% and specificity of 100% compared to endoscopy [66]. In a study of 23 patients [56], Koh et al. reported a per patient sensitivity and specificity of MRE of 91% and 71%. Finally, in a study of 33 patients [45] with two readers, Siddiki et al. reported MRE sensitivity and specificity of 86% and 67–78%.

Borthne and colleague [41] compared the sensitivity, specificity and diagnostic accuracy of MRE (300 mL mannitol in 15% water) and US to endoscopy in children with suspected IBD. They assessed wall thickness and contrast enhancement and found sensitivity of 81.8%, specificity 100% and diagnostic accuracy of 90% for MRE for CD. 50% of patients were willing to repeat the examination in future.

Diagnostic accuracy of MRE has also been compared to wireless capsule endoscopy (WCE). In one such study, Golder and colleagues detected the same number of inflammatory lesions in terminal ileum with both modalities but WCE detected additional lesions in proximal ileum and jejunum (12 vs. 1) whereas, MRE showed extra intestinal pathologies in 28% [42]. Two years later, Tillack et al [43] also compared MRE with WCE but only in known patients with CD. Both modalities showed the same disease features in 56% segments but WCE detected more superficial mucosal disease. However, MRE was better in diagnosing severe inflammatory muralchanges.

Sailer et al proposed an MRE score for post surgical recurrence, based on image quality, contrast enhancement, mural and extra mural bowel wall changes to assess post resection recurrence in CD.

MR0	No abnormal features
MR1	Minimal mucosal changes
MR2	Diffuse aphthoid ileitis, moderate recurrence
MR3	Severe recurrence with trans and extramural changes

MRE score by Sailer et al.

They used the previously validated Rutgreets score as a reference standard and high agreement was observed between MRE score and Rutgreets score [(44)].

The data in our study showed that the correlation between endoscopic SES-CD scoring and DWI scoring for disease activity was statistically significant (p value 0.03). Qualitative (visual inspection) assessment of DWI is a reasonably sensitive tool for detection of bowel inflammation in Crohn's disease based on a colonoscopic standard of reference but has poor specificity and cannot fully replace conventional sequences. In our patient cohort, DWI demonstrated a sensitivity of 92 % and a specificity of 42.8 % compared to colonoscopy, considering active disease on colonoscopy with SES -CD more than 5 and DWI score more than 1. Similar results demonstrated by Li et al. confirmed [(72)] that DWI could grade CD activity when compared to endoscopy as the reference standard. Kim et al. performed study [(73)] showed that positive DWI findings in the bowel were associated with higher CDEIS score.

The MRI parameters, which make up the scores, are of interest. Various parameters have been reported to correlate with disease activity with endoscopy as reference, particularly wall thickness (p value 0.025), contrast enhancement pattern (p value 0.049) and perienteric changes (p value 0.030). Florie et al [(39)] used water as intraluminal contrast medium and compared MRI with endoscopic grading of disease severity -CDEIS.

Wall thickness correlated moderately to strongly with CDEIS ($r=0.57, p<0.001$ and $r=0.50$, $p<0.001$) while enhancement correlated weakly to moderately ($r=0.45, p<0.001$ and $r=0.42$, $p<0.001$). In the same year, another study of MRE was performed at 3.0 T MRI and also used CDEIS as standard of reference [40]. Only a weak to moderate correlation was found between bowel wall thickness and CDEIS and between wall enhancement and CDEIS.

In our study, the correlation between DWI scoring and MRI MEGS scoring for disease activity was statistically significant (p value 0.002). Many workers have compared DWI with conventional MRI activity scores. Hordonneau et al, for example, [74] found the subjective presence of abnormal DWI had high sensitivity for segmental disease activity defined by a Maria score >7. Our data also suggested a relationship between DWI and an MRI activity score.

Finally, it should be noted that neither endoscopy nor pathology are truly adequate gold standards as MRE evaluates the entire length of the small bowel. For this reason, we only included the distal ileum in our analysis, however even the length of the terminal ileum evaluable by endoscopy varies between patients. The endoscopies were negative with some the cases demonstrating active disease on MRI, likely because the endoscopy simply did not reach that part of the distal ileum. In comparing endoscopy to MRE, we must use endoscopy as the gold standard. Therefore, all instances of discordance between the two modalities are recorded as a false MRI result, which may not be the case. This is necessary for statistical analysis but has the potential to bias our results against MRE.

SUMMARY AND CONCLUSION

1. The present study was conducted at the Department of Radiodiagnosis, Dayanand Medical College and Hospital, Ludhiana.

2. 32 patients with isolated ileal disease on colonoscopy were scanned on SIEMENS MAGNETOM SKYRA 48 CHANNEL 3 Tesla MRI.

3. Age range of the patients in the study was 17-77 years with mean age of 43.8 years with maximum patients more than 40 years of age.

4. 12 patients out of 32 had additional involvement of gastrointestinal segment in addition to ileal disease documented on colonoscopy.

5. Long segment and skip segment of bowel involvement was seen in 62.5% of the patients.

6. The correlation between clinical CDAI scoring and endoscopic SES-CD scoring for disease activity was very weak and not statistically significant with pearsman correlation coefficient of .313

7. The correlation between clinical CDAI scoring and MRI MEGS scoring for disease activity was very weak and not statistically significant.

8. The correlation between endoscopic SES-CD scoring and MRI MEGS scoring for disease activity was statistically significant (p value 0.007).

9. MRE demonstrated a sensitivity of 92 % and a specificity of 57.4 % compared to colonoscopy, considering active disease on colonoscopy with SES -CD more than 5 and MRI MEGS score more than 6.

10. The correlation between endoscopic SES-CD scoring and DWI grading for disease activity was statistically significant (p value 0.03).

11. Qualitative assessment of DWI has reasonably sensitivity of 92% for detection of bowel inflammation in Crohn's disease based on a colonoscopic standard of reference but has poor specificity of 42.8% and cannot fully replace conventional sequences.

12. The correlation between DWI scoring and MRI MEGS score for disease activity was statistically significant (p value 0.002).

13. The MRI parameters, which make up the scores were noted to correlate with disease activity with endoscopy as reference, particularly

wall thickness (p value 0.025), contrast enhancement pattern (p value 0.049) and perienteric changes (p value 0.030).

14. It should be noted that endoscopy is not truly adequate gold standard. Therefore, all instances of discordance between the two modalities are recorded as a false MRI result, which may not be the case. This is necessary for statistical analysis but has the potential to bias our results against MRE.

CONCLUSION

IBD is a lifelong condition that remains a diagnostic and therapeutic challenge and requires repeated assessment of disease extent and activity as part of management.

However, MRE has a positive diagnostic impact in patients under investigation for small bowel CD and significantly influences in therapeutic strategy of these patients.

MRE demonstrates excellent sensitivity, specificity and agreement compared to colonoscopy. Qualitative MRI scoring as well as individual MRI parameters correlate well with endoscopic disease activity (SES-CD), suggesting MRE a complementary tool to colonoscopy in the follow up of patients with colitis.

Qualitative (visual inspection) assessment of DWI is a reasonably sensitive tool for detection of bowel inflammation in Crohn's disease based on a colonoscopic standard of reference but has poor specificity and cannot fully replace conventional sequences. The value of DWI remains to be defined, but it may well have an adjunctive role in the assessment of disease activity and response evaluation. In those with known disease, rapid review of DWI could give a reasonable estimate of the overall active disease burden.

In summary, this thesis has shown MRI is a robust diagnostic technique, which has a valid clinical role in assessment of IBD. It can complement endoscopy and can act as biomarker of disease activity.

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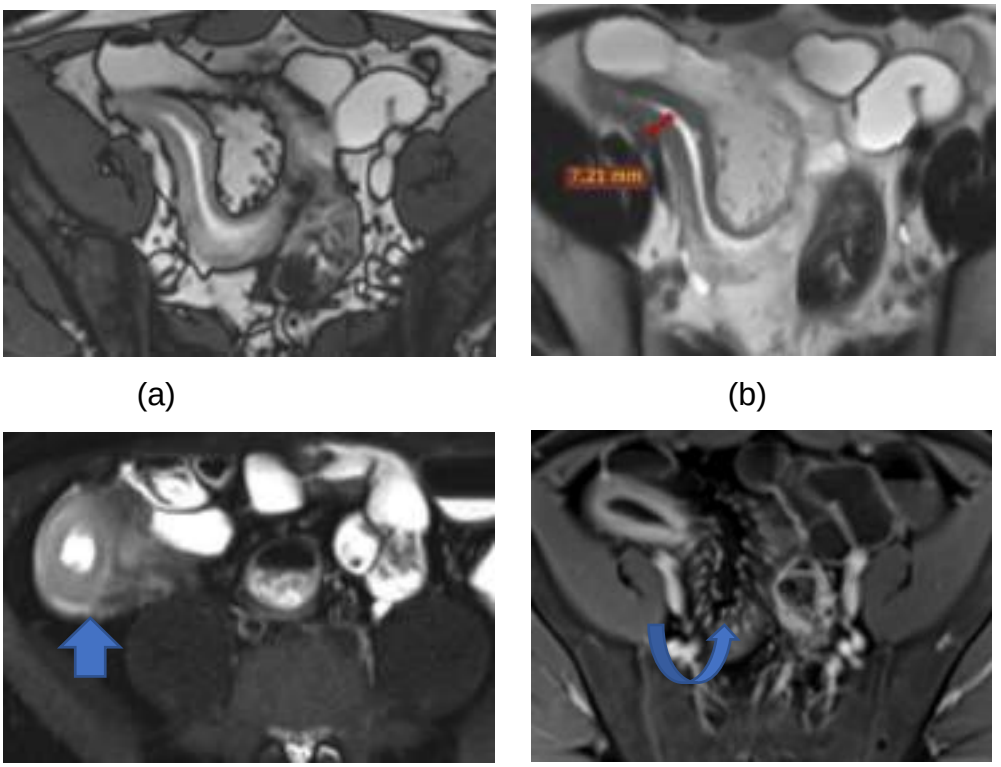
OBSERVATIONS

CASE 1 Severe Active Inflammatory stage of Crohn's disease in 25 year old male

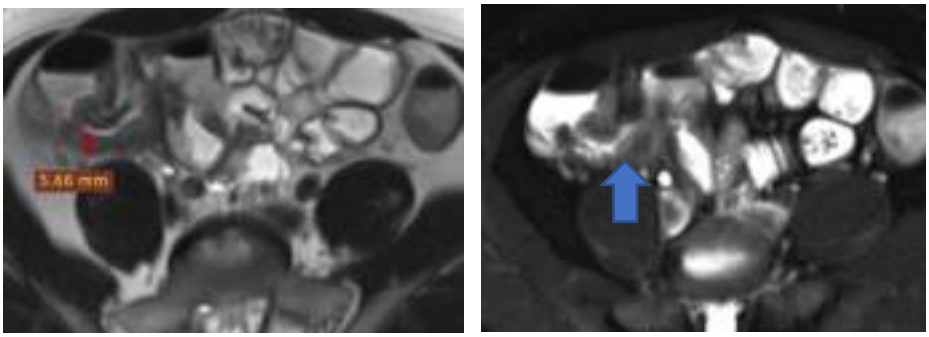


(a) (b)

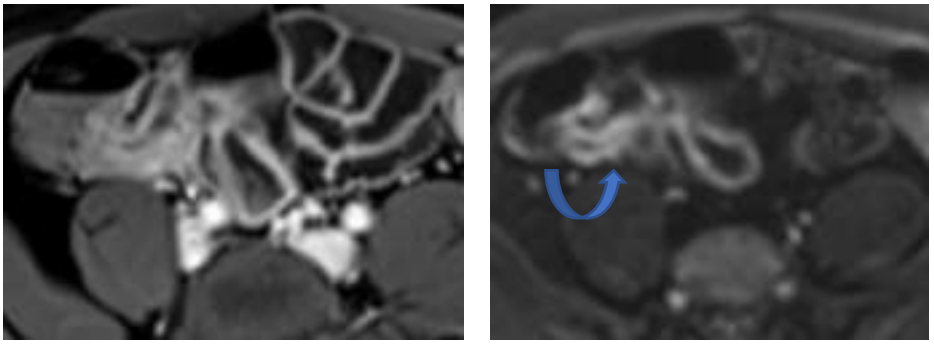
(c) (d)

(a) Axial TRUFI demonstrates long segment circumferential wall thickening of the terminal ileum. (b) Axial T2 HASTE shows marked wall thickening measuring upto 7mm. (red calipers) (c) Axial T2 FatSat shows hyperintense signal (straight arrow) of the diseased wall with significant perienteric changes. (d) Axial VIBE post contrast image shows grade 3 mural enhancement and prominent vasa recta giving comb's sign (curved arrow).

CASE 2 Moderate active inflammatory Crohn's disease in a 23 year old male



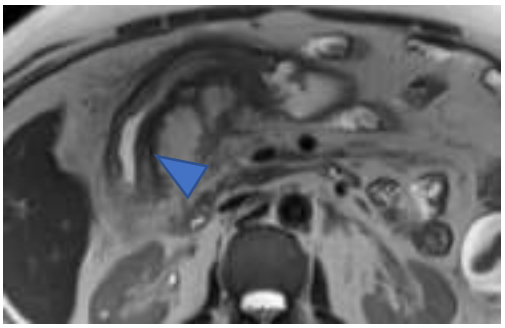
(a) (b)



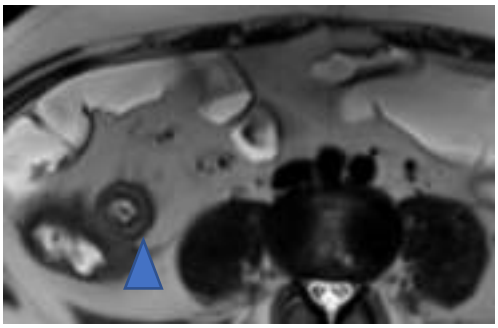
(c) (d)

(a) Axial T2 HASTE shows wall thickening of the terminal ileum measuring upto 5.6 mm (red calipers). (b) Axial T2 FatSat shows hyperintense signal (straight arrow) of the diseased wall with mild perienteric changes. (c) VIBE post contrast axial image shows increased mural enhancement. (d) DWI axial images show grade 3 mural signal abnormality (curved arrow) in the diseased segment.

CASE 3 Penetrating fistulizing crohn’s disease in a 64 year old male



(a)



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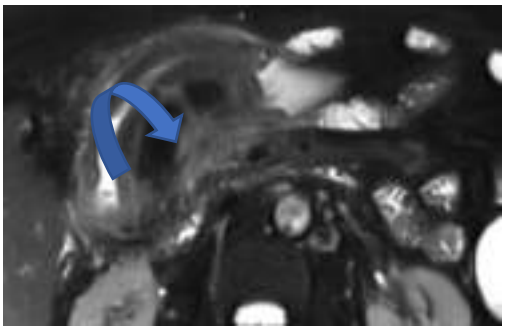
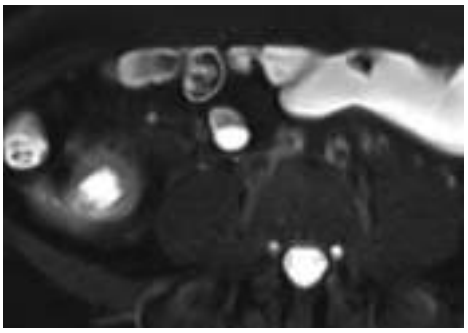


(c)



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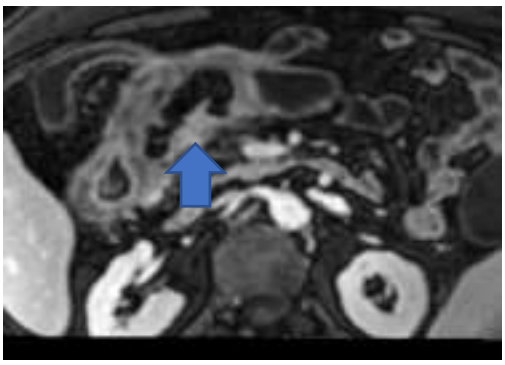
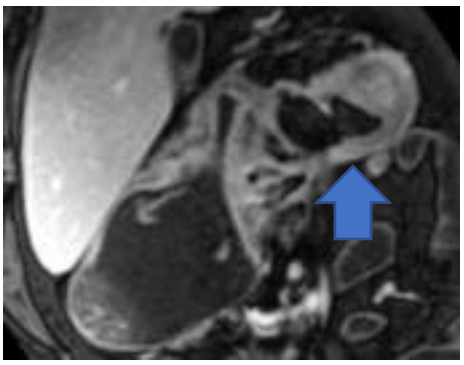


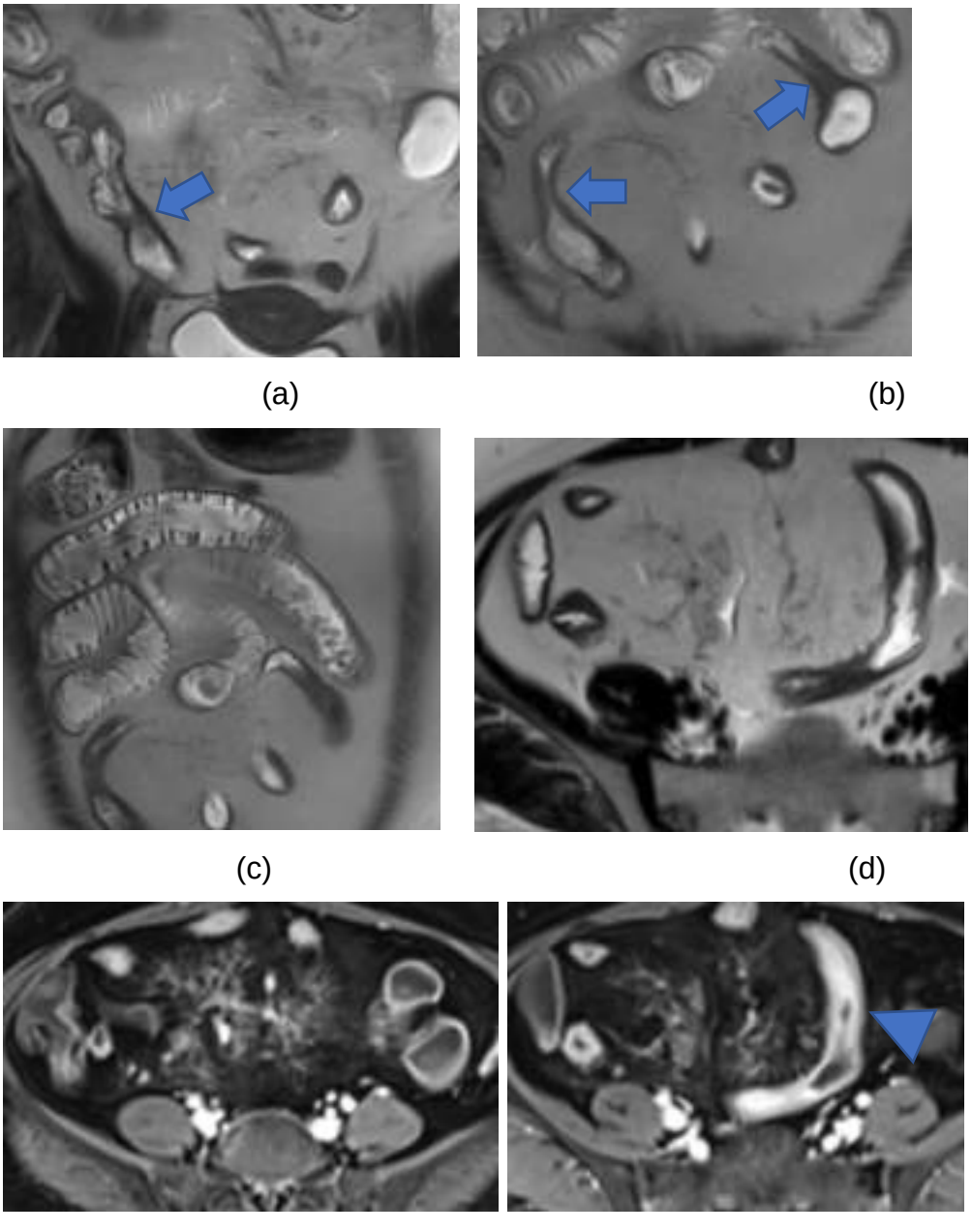
(e)



(f)

(a) , (b) T2 axial images show ileocolonic involvement with marked wall thickening of the diseased hepatic flexure and terminal ileum (arrowheads). (c), (d) T2 fatsat axial images show grade 2 perienteric changes (curved arrow) with hyperintense to intermediate mural signal intemsity. (e), (f) VIBE post contrast axial and reformatted coronal images show enhancing fluid filled tract suggesting colo- colic fistula (straight arrows).

CASE 4 Chronic fibrostenotic Crohn’s disease with low grade subacute intestinal obstruction in a 52 year old female



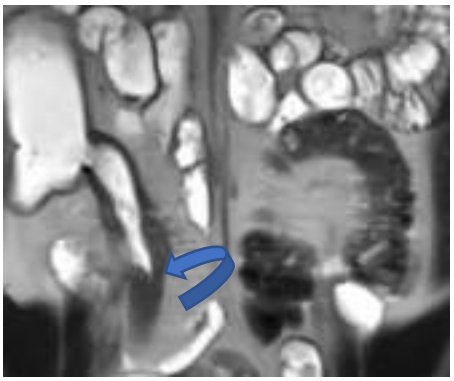
(a) (b)

(c) (d)

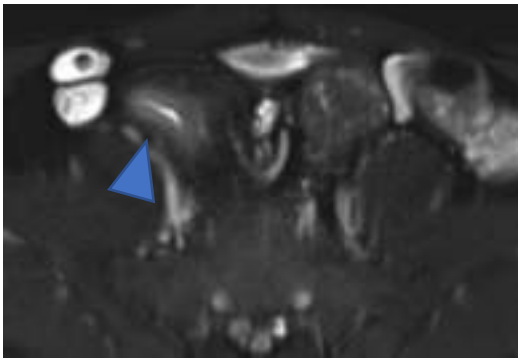
(e) (f)

(a), (b) Coronal T2 images show multiple skip segment involvement with mild wall thickening (straight arrows) of the terminal and distal ileum. (c) Coronal T2 images show upstream dilated small bowel loops suggestive of low grade intestinal obstruction. (d) T2 axial images show mild perienteric changes with fibrofatty proliferation. (e), (f) VIBE post contrast axial images show homogenous hyperenhancment of diseased ileum (arrowhead).

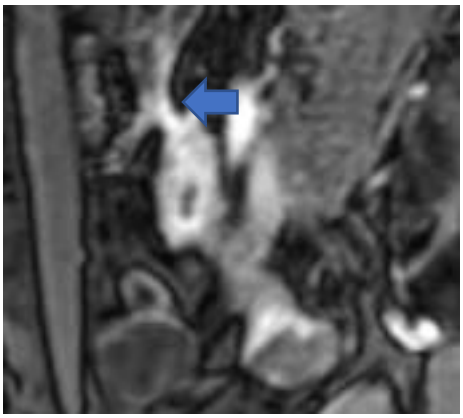
CASE 5 Penetrating fistulizing crohn’s disease in a 20 year old female



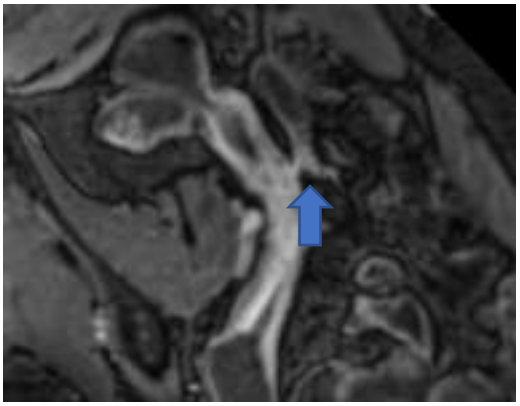
(a)



(b)



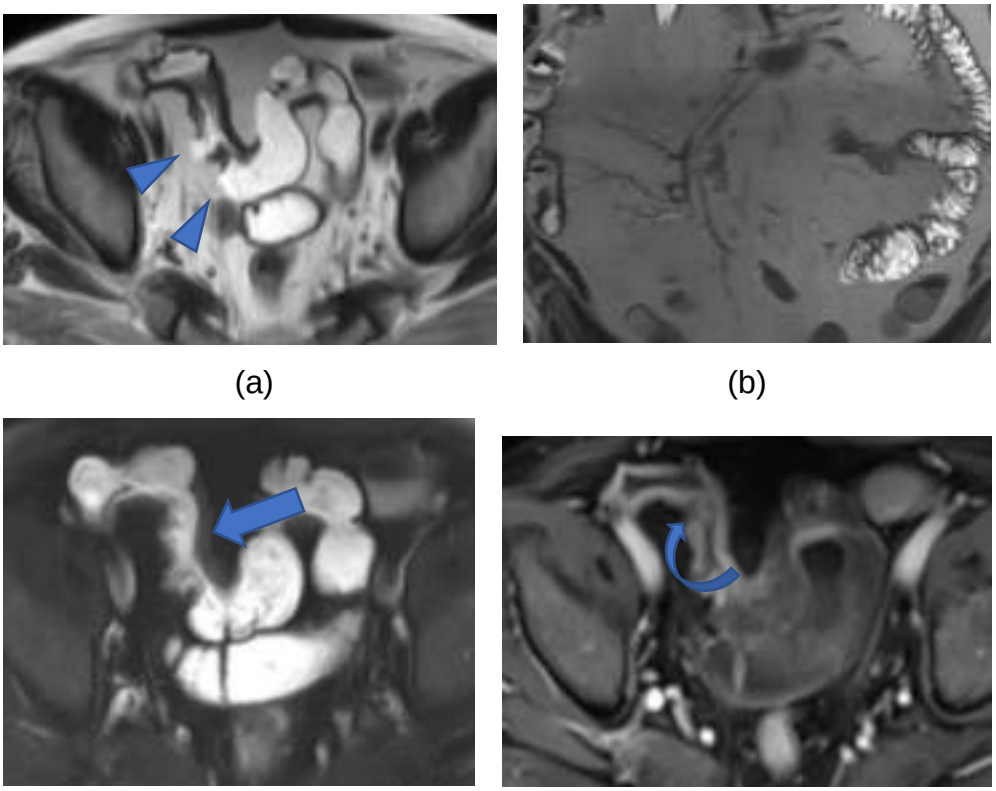
(c)



(d)

(a) Coronal T2 HASTE shows long segment wall thickening of the terminal ileum measuring upto 5.6 mm (curved arrow). (b) Axial T2 FatSat shows hyperintense signal (arrowhead) of the diseased wall with mild perienteric changes. (c), (d) VIBE post contrast sagittal and coronal images shows mural hyperenhancement with mural stratification with enhancing ileoileal fistula.

CASE 6 Chronic fibrostenotic Crohn's disease with pseudosacculations in a 64 year old male

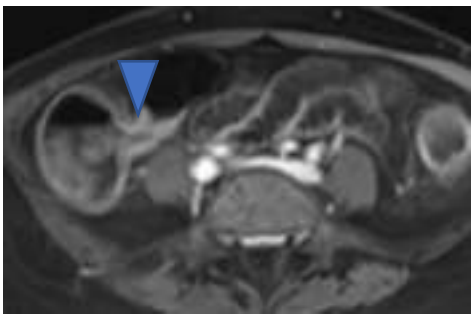


(a) (b)

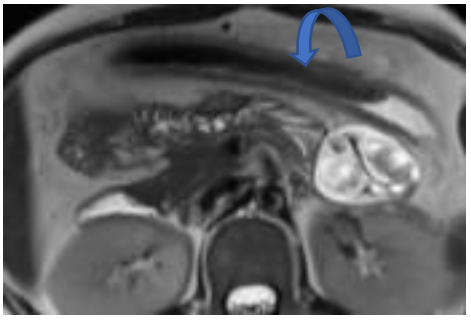
(c) (d)

(a) Axial T2 HASTE shows moderate wall thickening of the terminal ileum with pseudosacculations (arrowheads) along the anti mesenteric border. (b) Coronal T2 HASTE images show significant fibrofatty proliferation in the mesentery. (c) Axial T2 FatSat shows dark signal (straight arrow) of the diseased wall with no perienteric changes. (d) VIBE post contrast axial image shows grade 1 homogenous mural enhancement (curved arrow).

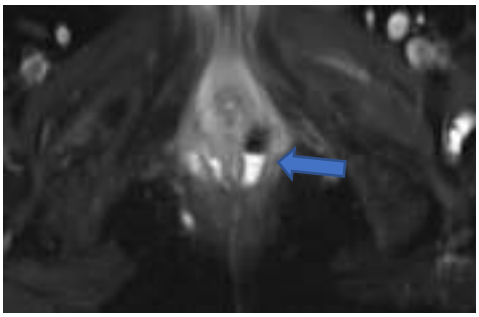
CASE 7 Severe active inflammatory Crohn's disease with perianal fistula in a 33 year old female



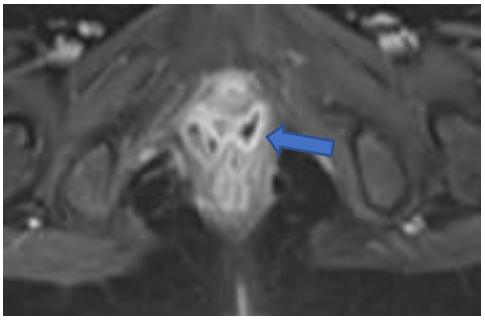
(a)



(b)



(c)



(d)

(a) VIBE post contrast axial image shows homogenously enhancing wall thickening (arrowhead) of the terminal ileum. (b) Axial T2 HASTE shows intermediate signal of the diseased colon with loss of haustra (curved arrow) and evident perienteric changes. (c) Axial T2 fatsat image and (d) VIBE post contrast axial image show complex perianal fistula (straight arrows).

KEY TO MASTER CHART

	ABBREVIATIONS
SES- CD	Endoscopic Crohn’s disease index
MEGS	Magnetic Resonance Enterography Global Score
DWI	diffusion weighted images
CDAI	Crohn’s disease activity index

S No.	Name	MRD No.	AGE	CDAI	Ileal SES CD	Ileal MEGS	DISEASE GRADING ON MRI	DWI SCORE ileal	Jejunum	Ileum	Ileocecal valve	Cecum	Appendix	Ascending Colon	Transverse Colon	Descending Colon	Sigmoid	Rectum	Anal Canal	Perianal Fistulae	Length of bowel involvement	Skip Segments
1	AK	128324	39	315	11	22	moderate	3	0	1	1	1	1	1	0	0	0	0	0	1	>15 cm	Yes
2	AG	636734	40	116	3	20	moderate	3	0	1	1	1	1	0	0	0	0	0	0	0	>15 cm	Yes
3	BS	722338	36	187	7	8	mild	3	0	1	1	0	0	0	0	0	0	0	0	0	<5cm	No
4	BR	137288	58	247	7	16	moderate	3	0	1	1	1	0	0	0	0	0	0	0	0	>15 cm	Yes
5	BL	21061	66	456	15	22	moderate	3	0	1	1	1	0	0	0	0	0	0	0	0	5-15cm	Yes
6	GM	670981	38	212	4	2	mild	1	0	1	0	0	0	0	1	0	0	0	0	0	5-15cm	Yes
7	GS	611715	26	321	14	24	moderate	3	0	1	1	0	0	0	0	0	0	0	0	1	>15 cm	No
8	NG	198872	65	256	8	12	mild	2	0	1	1	0	0	0	0	0	0	0	0	0	5-15cm	Yes
9	NS	666089	60	398	6	22	moderate	3	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	No
10	PK	644700	52	326	7	10	mild	3	0	1	0	0	0	0	0	0	0	0	0	0	<5cm	Yes
11	PSA	634696	70	294	7	7	mild	2	0	1	1	0	0	0	0	0	0	0	0	0	<5cm	No
12	RK	624759	42	304	6	4	mild	1	0	1	0	0	0	0	0	0	0	0	0	0	>15 cm	Yes
13	RD	173153	24	699	9	14	mild	3	0	1	0	0	0	0	0	0	0	0	0	0	>15 cm	Yes
14	SP	309671	21	141	9	30	severe	3	0	1	1	0	0	0	0	0	0	0	0	1	>15 cm	Yes
15	SS	638857	43	318	7	7	mild	1	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	Yes
16	SG	411787	58	142	10	24	moderate	3	0	1	1	1	0	0	0	0	0	0	0	0	>15 cm	No
17	SJ	728653	55	158	8	9	mild	2	0	1	1	0	0	0	0	0	0	0	0	0	5-15cm	No`
18	MK	416085	25	281	7	28	mild	3	1	1	1	0	0	0	0	0	0	0	0	0	>15 cm	No
19	RO	76325	28	383	8	5	mild	2	0	1	0	0	0	0	0	0	0	0	0	0	<5cm	No
20	AT	767673	17	338	7	13	mild	3	1	1	1	1	1	0	0	0	0	0	1	1	>15 cm	Yes
21	GS	733878	49	136	9	16	moderate	3	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	Yes
22	BM	830915	77	116	2	14	mild	3	0	1	0	0	0	0	0	0	0	0	0	0	>15 cm	Yes
23	BJ	823353	53	456	9	16	moderate	3	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	No
24	NJ	876574	32	111	3	6	mild	2	0	1	1	0	0	0	0	0	0	0	0	0	5-15cm	Yes
25	NR	797886	24	370	2	6	mild	1	1	1	0	1	1	0	0	0	0	0	0	0	<5cm	Yes
26	RC	799534	71	250	6	28	severe	3	0	1	1	1	0	0	0	0	0	0	0	0	>15 cm	Yes
27	VV	860205	23	240	10	15	moderate	3	0	1	1	0	0	0	0	0	0	0	0	1	5-15cm	Yes
28	SM	824671	50	295	8	24	moderate	3	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	Yes
29	MK	912357	40	119	8	28	severe	3	0	1	1	0	0	0	0	0	0	0	0	0	>15 cm	No
30	LS	910286	23	389	8	28	severe	3	0	1	0	0	0	0	0	0	0	0	1	1	>15 cm	No
31	ASK	272464	41	116	2	6	mild	2	0	1	0	0	0	0	0	0	1	0	0	0	<5cm	Yes
32	BPS	790639	55	251	3	8	mild	1	0	1	0	0	0	0	0	0	0	0	0	0	>15 cm	No`

S No.	Name	MRD No.	T2 signal	Wall thickness in mm	Ulcers	Wall enhancement	Enhancement Pattern	Comb's Sign	Fibrofatty proliferation	Perienteric changes	Fistulae/ Sinus	Pliability	Lymphadenopathy	Abscess	Obstruction
1	AK	128324	Intermediate	10	No	grade3	Mural, stratified	YES	YES	YES	YES	Reduced	Present	NO	NO
2	AG	636734	Intermediate	6.5	No	grade2	Mural, stratified	YES	YES	NO	NO	Reduced	Present	NO	NO
3	BS	722338	Intermediate	7	No	grade3	homogenous	NO	YES	NO	NO	Reduced	Present	NO	NO
4	BR	137288	Intermediate	10	No	grade2	Mural, stratified	YES	YES	NO	NO	Reduced	Present	NO	NO
5	BL	21061	Hyperintense	10	Yes	grade3	Mural, stratified	YES	NO	NO	NO	Preserved	Absent	NO	NO
6	GM	670981	dark	2	No	grade1	homogenous	NO	YES	NO	NO	Reduced	Absent	NO	NO
7	GS	611715	Hyperintense	9	No	grade2	homogenous	YES	YES	YES	YES	Reduced	Absent	NO	NO
8	NG	198872	Intermediate	7	Yes	grade2	Mural, stratified	YES	YES	NO	NO	Reduced	Absent	NO	NO
9	NS	666089	Hyperintense	9	No	grade3	Mural, stratified	YES	YES	NO	NO	Reduced	Absent	NO	NO
10	PK	644700	Hyperintense	9	No	grade2	Mural, stratified	YES	YES	NO	NO	Reduced	absent	NO	YES
11	PSA	634696	Intermediate	5	No	grade1	Mural, stratified	NO	NO	NO	NO	Reduced	Present	NO	NO
12	RK	624759	dark	4	No	grade1	homogenous	YES	NO	NO	NO	Preserved	Absent	NO	NO
13	RD	173153	Intermediate	6	No	grade1	homogenous	YES	NO	YES	NO	Reduced	Absent	NO	NO
14	SP	309671	Hyperintense	8	No	grade3	Mural, stratified	YES	YES	YES	YES	Reduced	Absent	NO	YES
15	SS	638857	dark	4	No	grade1	homogenous	NO	NO	NO	NO	Reduced	Present	NO	NO
16	SG	411787	Intermediate	8	Yes	grade3	Mural, stratified	YES	YES	YES	NO	Reduced	present	NO	NO
17	SJ	728653	dark	5	No	grade3	homogenous	NO	NO	NO	NO	Reduced	present	NO	NO
18	MK	416085	Hyperintense	12	No	grade3	Mural, stratified	YES	YES	YES	NO	Reduced	absent	NO	NO
19	RO	76325	dark	7	No	grade1	homogenous	NO	NO	NO	NO	Preserved	absent	NO	NO
20	AT	767673	Hyperintense	12	No	grade2	Mural, stratified	YES	NO	YES	YES	Reduced	absent	NO	NO
21	GS	733878	Intermediate	6	Yes	grade2	Mural, stratified	YES	NO	NO	NO	Reduced	Present	NO	NO
22	BM	830915	dark	6	No	grade3	homogenous	YES	YES	NO	NO	Reduced	Absent	NO	NO
23	BJ	823353	Intermediate	6	Yes	grade2	Mural, stratified	YES	YES	NO	NO	Reduced	Present	NO	NO
24	NJ	876574	dark	5	No	grade1	homogenous	YES	YES	NO	NO	Reduced	Absent	NO	NO
25	NR	797886	Intermediate	5	No	grade2	homogenous	YES	NO	NO	NO	Reduced	Present	NO	NO
26	RC	799534	Hyperintense	8	Yes	grade3	Mural, stratified	YES	YES	YES	NO	Reduced	Present	NO	YES
27	VV	860205	Intermediate	6	No	grade2	Mural, stratified	YES	YES	YES	YES	Reduced	Present	NO	NO
28	SM	824671	Hyperintense	8	Yes	grade3	Mural, stratified	YES	YES	YES	NO	Reduced	Absent	NO	NO
29	MK	912357	Hyperintense	8	Yes	grade3	Mural, stratified	YES	YES	YES	NO	Reduced	Present	NO	NO
30	LS	910286	Hyperintense	7	Yes	grade2	Mural, stratified	YES	NO	YES	YES	Reduced	Absent	NO	NO
31	ASK	272464	Intermediate	4	No	grade2	homogenous	YES	YES	NO	NO	Reduced	Present	NO	NO
32	BPS	790639	Intermediate	5	Yes	grade1	homogenous	YES	YES	NO	NO	Preserved	Present	NO	NO

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Date 9/4/2021

The Principal,
DMC,Ludhiana

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr.Yogita Nevtia**, a student of your college for **MD Radio-Diagnosis** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Profile of mr enterography in crohn's disease

Supervisor
Dr. Archana Ahluwalia
Prof.,
Dept. of Radio-Diagnosis,
DMCH, Ludhiana.

Co-Supervisor
Dr. Chandan Kakkar
Assoc. Prof.,
Dept. of Radio-diagnosis,
DMCH, Ludhiana.

Dr. Varun Mehta
Prof.,
Dept. of Gastroenterology,

The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

S P Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

RADIODIAGNOSIS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

November, 2019

Dr. Yogita Nevtia

DEPARTMENT OF RADIODIAGNOSIS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE
For the degree of	RADIODIAGNOSIS
Name of the candidate	Dr. Yogita Nevtia
Supervisor	Dr Archana Ahluwalia , Professor, Department of Radiodiagnosis , DMCH , Ludhiana
Co-supervisor	Dr Chandan Kakkar, Associate Professor Department of Radiodiagnosis , DMCH , Ludhiana Dr Varun Mehta, Professor, Department of gastroenterology, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Crohn's disease is a chronic inflammatory disease of gastrointestinal tract of unknown etiology with a disease course of recuurent flares and remissions. Internationally, the incidence is 0.1-16 cases per 100,000 person-years for Crohn's disease. The management of IBD and assessment of response to therapy largely depends on documenting the location, extent and severity of inflammation. MR Enterography has largely emerged as a non-invasive radiation free modality providing simultaneous information about mural and extramural features dictating its therapeutic strategy influencing impact in patients with Crohn's disease.

Aim of Study: To evaluate the profile of MR Enterography in assessing the extent and disease activity in patients with Crohn's disease and correlate with endoscopic, histological, clinical and lab parameters.

Materials& methods: A prospective study will be done on patients of clinically diagnosed Crohn's disease referred for MR Enterography to department of radiodiagnosis, DMCH, Ludhiana over a period extending from 1 Dec,2019 to 31 May,2021.

Clinical Significance:

The clinical usefulness is emphasized by the need for multiple imaging examinations in Crohn's disease. MR Enterography is a non-invasive radiation free modality especially useful in young and female patients. Therapeutic strategy aims to achieve full remission which requires accurate serial documentation of disease activity. MR Enterography can differentiate acute inflammation from fibrosis due to better soft tissue contrast. DWI sequence can have to potential to avoid contrast enhanced sequences specially in patients with compromised renal function.

Keywords: MR enterography, crohn's, Diffusion weighted imaging, cine.

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE"** exist in the Department of Radiodiagnosis, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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Professor
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Co-Supervisor

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Associate professor
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Dr. KavitaSaggar
Professor and head
Department of Radiodiagnosis
DMCH, Ludhiana

Place : _____

Date : _____

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Yogita Nevtia
Department	Radiodiagnosis
Topic of Thesis	Profile of MR Enterography in Crohn's disease
Likely date of appearing in PG examination	May,2022
Date of enrollment	1 MAY, 2019
Name of Head of Department	Dr. Kavita Saggar
1) Supervisor **2) Co-Supervisor**	Dr. Archana Ahluwalia Dr. Chandan Kakkar Dr. Varun Mehta
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Assistant Dean Academics)	Dr. Deepinder K Chhina (Professor & Head, Microbiology)
Dr. Rajoo Singh Chhina (Dean Academics)	Dr. Neena Sood (Professor & Head, Pathology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. YOGITA NEVTIA D/O ANITA NAND NEVTIA ABOVE YES BANK NEAR HDFC BANK P.N.B. ROAD BUDHLADA, DISTT MANSA -151502
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	M.D. RADIODIAGNOSIS
4	DATE OF ADMISSION OF COURSE	1 MAY, 2019
5	TITLE OF THE TOPIC	ROLE OF MR ENTEROGRAPHY IN CROHN'S DISEASE

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Crohn's disease occurs in the young adulthood with evident background genetic and environmental risk factors and autoimmune pathogenesis. It undergoes a waxing and waning course with cumulative structural damage to the bowel with a progression from inflammation to penetrating disease and fibrosis over time. Although life expectancy is near to mean of healthy population it deteriorates the heath related quality of life due to chronic nature of disease, extra-intestinal manifestations and complications, effect of medical and surgical treatments and their side effects and stress of developing cancer. There is increasing emphasis on accurately documenting disease phenotype and tracking it over time. There is need to accurately assess biological activity and changes in response to therapy.

Conventional endoscopy with biopsy is invasive and can only evaluate colon and few centimeters of ileum with little information about transmural and extra-enteric extent. It is also frequently limited by colonic strictures. Cross-sectional imaging in the form of CT and MR enterography are therefore of increasing importance in the management of Crohn disease, providing information on disease extent, biological activity, complications, and bowel damage. The Lémann score, for example, is aimed at measuring long-term damage to the bowel over time and cross-sectional imaging findings such as wall thickening, abscess, fistula, and bowel dilatation are fundamental to the score.

The use of immunosuppressive therapy must be guided by objective evidence of biological activity. Clinical scores based on patient symptoms, such as Crohn disease activity index (CDAI) and Harvey-Bradshaw index (HBI), are widely used in clinical trials but are subjective and do not truly reflect underlying biologic disease activity [1] and rarely correlate well with more objective biochemical inflammatory markers, such as CRP measurement and endoscopic grading of disease activity. Blood markers such as WBC count and CRP concentration are sensitive for inflammation, but values may be elevated in infections and other chronic inflammatory conditions. Faecal markers such as calprotectin and lactoferrin are sensitive for mucosal

inflammation but are not specific to inflammatory bowel disease and may be elevated in bowel infections and neoplasia.[2] Widely used endoscopic scores include the Crohn disease endoscopic index of severity (CDEIS) and the simple endoscopic score for Crohn disease (SES-CD). These endoscopic scores correlate well with mural disease activity. MRI features are consistently related to disease activity such as mural thickness and T1 enhancement. Extramural features of inflammation such as comb sign, lymph enlargement and fat wrapping are also useful, although their association with disease activity is less consistent in the literature. Endoscopy is the current reference standard for MR enterography to assess its diagnostic efficacy.

Until the advent of MRE, CT enterography remained the imaging modality of choice. CT enterography is widely available, affordable and accessible to masses with shorter examination time, fewer motion artifacts and better spatial resolution.[3] However, MRE remains better in differentiating active inflammation from fibrosis. Main benefits of MRE are – improved soft tissue contrast, lack of radiation, ability to repeatedly image an affected bowel segment over a period of time and dynamic / cine imaging to assess bowel motility. Cipriano et al even evaluated the cost-effectiveness of MRE over CTE in reducing the patients' life-time risk of developing cancer. Fast T2 weighted MR cine sequence such TrueFISP permits rapid acquisition of images on the same plane within a single breath holding time resulting in high temoral resolution of bowel motility. Both acute and chronic diseased segments have abnormal bowel motility. Some semi-automatic softwares can plot luminal diameter over time and a significant negative correlation has been found between motility and histopathological scores.

Advantages of MR enterography over endoscopy:-

-Spotting mural, extramural as well as extraenteric findings and staging extent and disease activity guiding an appropriate medical and surgical approach.

-Aiming to achieve remission of mural disease which can still exist in spite of endoscopically documented healed mucosa.

-Acceptance of MRE by patients with regard ,to invasiveness of endoscopy repeated in follow ups during therapeutic response assessment.

DWI is a specialized technique that maps the diffusion of water molecules in biologic tissue. Inflamed bowel wall shows DR with associated decrease in

ADC values presumably as a result of infiltration of inflammatory cells, dilated lymphatic channels and development of granulomas resulting in narrowed extracellular space. DWI for bowel can be acquired with breath hold, free breathing or with respiratory triggering. It can be utilized in 3 ways- detection of inflamed bowel segment, assessment of complications like fistula and abscess and detection of lymph nodes. In future it might replace post gadolinium imaging for detection of inflammation because it doesn't use IV contrast and can provide a quantitative index i.e. ADC in addition to imaging. DWI has the potential to become a tool for quantitative assessment and therapeutic response assessment. However, there are conflicting results regarding routine replacement of conventional contrast enhanced MR enterography with DWI. There are evidences of low specificity which make it unclear whether the reported instances of additional disease visible only on DWI actually represented true-positive findings in areas with subtle inflammation below the resolution of MR enterography [4] or merely a fortuitous coincidence of DWI false-positives due to inadequately distended bowel segments. DWI might find a potential role as a substitute for iv contrast injection in pregnant patients, patients with high risk for contrast allergy and impaired renal function carrying a risk of nephrogenic systemic sclerosis.

Introduction of biologics and immunosuppressive agents have changed the treatment goals from symptomatic control to complete mucosal healing defined as sustained deep remission. However, mural inflammation can still exist in the context of a healed mucosa.[5] Reduction of wall thickening, enhancement and T2 signal intensity on MRI are seen after therapy. With introduction of aggressive treatment options, quantification of such changes on MR enterography might be required to accurately document treatment response as it might prove superior to using mucosal healing as an endpoint of therapeutic response.

MRI activity scores can at least complement and potentially replace conventional clinical and endoscopic indexes for patient triage and assessment of therapeutic efficacy. A sound communication between radiologists and gastroenterologist can help determine the potential of MRI in the management of this life-long debilitating disease.

6.2 REVIEW OF LITERATURE

Magnano and colleagues compared MRE, US and Doppler US using ileocolonoscopy as reference standard in children with known CD. MRE was performed after oral intake of polyethylene glycol solution. It depicted stenosis, thickening and hyperemia of bowel wall. Concordance of MR and US for detection of wall thickening and increased vascularity was 95% and 80% respectively.[6]

Florie et al used water as intraluminal contrast medium and compared MRI with endoscopic grading of disease severity -CDEIS. Wall thickness correlated moderately to strongly with CDEIS ($r=0.57, p<0.001$ and $r=0.50$, $p<0.001$) while enhancement correlated weakly to moderately ($r=0.45, p<0.001$ and $r=0.42$, $p<0.001$).[7] They also compared patient experience and overall preference. Patients found endoscopy more painful and hence, expressed preference for MRE as future investigation. In the same year, another study of MRE was performed at 3.0 T MRI and also used CDEIS as standard of reference.[8] Only a weak to moderate correlation was found between bowel wall thickness and CDEIS and between wall enhancement and CDEIS. Again the majority patients preferred MRE to ileocolonoscopy.

Borthne and colleague compared the sensitivity, specificity and diagnostic accuracy of MRE (300 mL mannitol in 15% water) and US to endoscopy in children with suspected IBD. They assessed wall thickness and contrast enhancement and found sensitivity of 81.8%, specificity 100% and diagnostic accuracy of 90% for MRE for CD. 50% of patients were willing to repeat the examination in future.[9]

The ability of MRE to precisely detect active small bowel disease has been compared with CTE by using endoscopy as reference standard. In one such study in 2009, a similar sensitivity of 90.5% for MR enterography and 95.2% for CT enterography (p 0.32) was reported for detection of active disease and both modalities diagnosed additional disease in 24% of patients who had normal ileocolonoscopy.[10] A few years later, Fiorino and colleagues again used ileocolonoscopy as reference standard to compare both modalities and reported supremacy of MRE in the recognition of strictures ($p=0.04$).[11]

Laghi et al derived an MRE score based on wall thickness and contrast enhancement in children with known CD use CDAI as a global reference standard together with ileocolonoscopy to evaluate disease activity in terminal ileum. They used polyethylene glycol as the oral agent. This score exhibited sensitivity of 84% and specificity of 100% for recognition of erosive ileitis seen on endoscopy.[12]

Pilleul et al in 2005 again verified positive correlation between bowel wall thickness and paediatric CDAI on MRE with 5% mannitol but no significant correlation was established with contrast enhancement.[13] MRE also revealed fistulae [9], strictures [8] and intussusception [1] in these patients.

Zappa and colleagues in a retrospective study compared the mural and extra mural findings of pre-operative MRE with the pathological analysis in resected specimen in 53 known patients of CD. The MRE parameters significantly associated with inflammation were wall thickness, wall enhancement, pattern of enhancement, T2 relative hyper signal, blurred wall enhancement, comb sign, fistula and abscess.[14]

Low and colleagues used multiple reference standards including surgical, endoscopic and histological findings together with barium studies to compare MRI and CT. MRI was performed with 2% oral barium sulfate, rectal water and IV gadolinium while IV contrast enhanced CT was performed with positive and negative enteral contrast in equal number of patients. Based on wall thickness and contrast enhancement on MRE was found superior to CT in depicting disease (85% vs. 65% abnormal segments). It was not only better in depicting mild disease (79% vs. 49% segments) but also in delineating mural thickening (41% vs. 11% segments) and mural enhancement (89% vs. 11% segments).[15] Koh et al assessed bowel wall thickness, contrast enhancement and perienteric changes on MRE (with oral water) in comparison to CDAI, endoscopy and surgery. MRE had overall sensitivity of 91% and specificity of 71% on per patient basis while CDAI had sensitivity of 92% and specificity of 28% for active disease.[16]

A study including 40 patients compared the detection of abnormalities with and without cine MRI. Overall, cine MRI depicted 35 more Crohn disease–related findings than did MRI performed with the standard protocol (p = 0.007).[17] In a 2012 study, 28 patients with Crohn disease underwent cine

MRI with true fast imaging with steady-state precession (true FISP) sequences, and a software- quantified motility index was derived from the terminal ileum. Inflammatory activity was graded with a histologic score from terminal ileal biopsy (endoscopic acute inflammation score [eAIS]). Terminal ileal motility correlated negatively with eAIS ($r = -0.52$, $p = 0.005$) and with an MRI activity score based on conventional parameters such as wall thickness and T2 signal intensity ($r = -0.7$, $p < 0.001$).[18]

In the derivation study, 50 patients with established Crohn disease underwent colonoscopy and 3-T MRI within 2 days. Binary logistic regression was used to define MRI features (e.g., wall thickness, edema, ulceration, pseudopolyps, and relative contrast enhancement) that were independent predictors of endoscopic disease activity and ulceration. Wall thickness ($p = 0.007$), relative contrast enhancement ($p = 0.01$), mural edema ($p = 0.02$), and ulceration at MRI ($p = 0.003$) were independent predictors of segmental CDEIS. On the basis of their regression model, the authors proposed a simplified MaRIA score per segment: 1.56 × wall thickness in millimeters + 0.02 × relative contrast enhancement + 5 × edema + 10 × ulceration. The MaRIA score had good correlation with the segmental CDEIS ($r = 0.81$, $p < 0.001$). A global MaRIA score calculated by adding individual segmental scores also had significant correlation with total CDEIS ($r = 0.78$), CRP concentration ($r = 0.53$), and HBI ($r = 0.56$). Importantly, the authors subsequently validated the MaRIA score in a new cohort of 48 patients.[19] Using the same MRI protocol and CDEIS reference, they found that the segmental MaRIA score again correlated strongly with CDEIS ($r = 0.80$, $p < 0.001$) and that the global MaRIA score correlated with the CDEIS ($r = 0.837$), CRP concentration ($r = 0.413$), and HBI ($r = 0.42$).

In a retrospective study that included 120 patients who underwent MRE for known or suspected Crohn disease [20], active disease was found in 57.5% of patients; 53% of the patients underwent additional medical treatment of active disease found with MRE, and 16% underwent surgery. Intraoperative findings were consistent with the MRE diagnosis. In a study that included 51 patients[21], the MRI findings markedly changed the diagnostic confidence of clinicians about the presence of small-bowel disease and their assessment of current disease activity, disease extent, and extramural complications. In that

study, the MRI findings led to a change in the planned therapeutic strategy for 61% of patients.

Zippi et al. proposed an MRI score that considers the overall degree of wall inflammation (graded 0–3),wall thickness, and length of diseased bowel and correlated this with fecal calprotectin content as a global marker of disease activity.[22] Positive correlation was found between MRI wall inflammation and wall thickness and calprotectin content but not between length of diseased bowel and calprotectin content. Also using a reference standard of fecal calprotectin content, Makanyanga et al. tested a global MRI score composed of qualitatively graded small-bowel and colonic wall thickness, mural T2 signal intensity, perimural T2 signal intensity, T1 enhancement, and enhancement pattern but including an assessment of length of diseased bowel and extramural features (comb sign, lymph nodes, fistulas, and abscesses).[23] In 27 patients with Crohn disease, the total MRI score correlated significantly with fecal calprotectin content (Kendall τ, b = 0.37, p = 0.01).

The MaRIA score was used to evaluate treatment-induced changes in 27 patients after 12 weeks of corticosteroid or adalimumab therapy with ileocolonoscopy (CDEIS) as a reference standard. A Ma-RIA score less than 40 was predictive of endoscopic remission with a sensitivity of 82% and specificity of 85%

There are a few studies that performed DWI examinations in patients with IBD without oral fluid contrast agent, with variable results. Because good fluid distention of the bowel is generally considered essential for a successful enterographic examination, administration of luminal fluid contrast agent is generally recommended as the standard procedure for MR enterography.[22] Therefore, there is probably no good reason not to use oral fluid contrast agent for DWI examination of the bowel in patients with Crohn disease, even if a few studies have shown the technical feasibility of DWI examination without it.

According to a recent systematic review and meta-analysis[10], which assessed the research studies published through March 31, 2015, the diagnostic performance of DWI enterography (performed after administration of oral fluid contrast agent) for active bowel inflammation in Crohn disease has been very heterogeneous, with the reported sensitivities and specificities

ranging from 68% to 100% (Higgins I^2 = 87.9%) and from 51% to 100% (Higgins I^2 = 95.1%), respectively. Of note, some studies likely overestimated the accuracy of DWI enterography for diagnosing active bowel inflammation by not using appropriate reader blinding when interpreting DWI or by using conventional contrast enhanced MR enterography as the reference standard, rather than external reference standards, such as endoscopy. That systematic review also suggested that the meta-analytic summary estimates of 79% sensitivity and 61% specificity, which were obtained from studies without such sources of bias, may be regarded as conservative estimates of the diagnostic accuracy of DWI enterography. False positives tend to occur in bowel loops with inadequate fluid distention, particularly in the colorectum and jejunum. Because the large intestine is often not well distended with fluid or contains a large amount of air when standard MR enterography is performed, some investigators have used a rectal water enema to avoid this limitation.[24] It would be interesting to determine whether DWI false-positives could be significantly decreased by using a water enema. One study also reported that lymphoid nodular hyperplasia of the terminal ileum, which is an incidental normal variant that is typically observed in children and adolescents, can lead to false-positive results on DWI enterography, in addition to mimicking inflammatory mural findings on conventional contrast-enhanced MRE.

The correlation between the degree of mural diffusion restriction assessed using DWI enterography and the severity of the bowel inflammation in Crohn disease suggests that DWI enterography may have a potential role in quantitative assessment. The primary purposes of such quantitative assessment include stratification of patients according to inflammation severity for prescribing customized treatments and the ability to monitor changes in the severity of bowel inflammation after treatment. The technical reproducibility (or lack thereof) of this quantitative approach needs to be clarified. Unlike visual evaluation of DW images, which is somewhat crude but fairly robust, quantitative ADC measurement is well known to have some variability in various applications in the abdomen. For example, according to one study, ADC values measured in malignant hepatic tumors can change as much as 30% merely as a result of scan-rescan variability and without any real changes. The differences caused by different scanning techniques and

parameters, interscanner variability, and within-scanner variability (i.e., different ADC values even when the same subject is scanned repeatedly using the same scanner and the same scanning parameters) are well-established sources of variability in quantitative measurements using DWI. Therefore, clinical application of the quantitative parameters obtained using DWI enterography has yet to be determined. In addition, considering the narrow width of the bowel wall and the presence of multiple diseased segments in typical patients with Crohn disease, measuring the ADC values using ROIs is expected to be more difficult and may be inclined to greater observer variability compared with ADC measurements in tumor masses or in solid organs. Therefore, although several studies have reported high interobserver reproducibility in measuring the ADC values from the bowel wall in patients with Crohn disease when using a given image set, this may require further validation if the same consistency among readers can be more widely achieved in daily clinical practice outside the controlled research settings.

The role of DWI enterography for post-therapeutic monitoring of inflammatory activity in Crohn disease can be more directly and clearly evaluated by the use of longitudinal follow-up studies. Retrospectively analyzed 17 patients with Crohn disease who had been monitored using DWI enterography after therapy with tumor necrosis factor–α antagonist.[25] That study showed that ADC values measured in the bowel wall significantly increased in clinical responders but did not change significantly in clinical nonresponders.

A few small studies, consisting of five to 20 patients each, performed correlational analyses between intestinal mural ADC values obtained on preoperative DWI enterography and the pathologic findings in surgically resected bowel specimens. Those studies reported an additional association between decreased mural ADC values and mural fibrosis. Because active bowel inflammation often coexists with fibrosis, the presence of fibrosis might be a confounder in assessing bowel inflammation using DWI. The relative effect of mural inflammation and fibrosis on the diffusion restriction in Crohn disease may require further determination in future larger studies.

6.3 AIMS AND OBJECTIVES OF THE STUDY

To evaluate the profile of MR Enterography in assessing the extent and disease activity in patients with Crohn's disease and correlate with endoscopic, histological, clinical and lab parameters.

7. MATERIALS AND METHODS

7.1 Source of Data

A prospective study will be done on patients of clinically diagnosed Crohn's disease referred for MR Enterography to department of radiodiagnosis, DMCH, Ludhiana over a period extending from 1 Dec,2019 to 31 May,2021.

7.2 METHOD OF COLLECTION OF DATA

Written consent will be obtained from each patient after explaining the procedure in his/her vernacular language to allay fear and anxiety. A detailed relevant history about onset, duration, nature and frequency of abnormal bowel habits and abdominal complaints will be recorded in a pre-designed performa. Record of previous imaging, biopsy, endoscopic and biochemical investigations will be evaluated for overall correlation.

Patients will be subjected to a multiplanar, multisequential MRI scan of prepared bowel on a MAGNETOM SKYRA 48 channel 3 TESLA MR Machine by Siemens, Germany.

INCLUSION CRITERIA:

Patients with clinically diagnosed Crohn's disease.

EXCLUSION CRITERIA

- Patients with high grade bowel obstruction.
- General contraindications to MRI (cardiac pacemaker, metallic implants, severe claustrophobia, cochlear implants).
- Patients with history of contrast allergy or renal impairment.
- Patients who do not consent to be a part of the study.

PREPARATION OF THE PATIENT

The patients will be asked to come after 4 hrs fasting. On arrival at the radiology department, patient will be asked to drink 800 ml PEG solution over 50 min.

Polyethylene glycol (PEG LEC) solution is prepared by dissolving PEG with electrolytes & flavoring agents (pineapple and orange) which is commercially available as PEG LEC 137.15 grams of powder in 2 litres of water. The oral contrast material will be divided into two portions, and instructed to drink each portion in 25 minutes. To opacify stomach and duodenum just before imaging, patients will be instructed to have another 200 ml of oral contrast. Patient will

be instructed to drink the solution gradually for even distension of the entire small bowel.

One hour after the commencement of oral contrast ingestion patient will be imaged on **MAGNETOM SKYRA 48 channel 3 TESLA MR Machine by Siemens, Germany** using phased array abdomen coil in supine position. Patient will be instructed for breathing instructions.

After running the kinematic sequences and just before iv contrast enhancement sequences 1mg of i.v buscopan each will be given to minimize movement artifact from peristalsis. Images are obtained.

MAGNETIC RESONANCE IMAGING PROTOCOL:

SEQUENCES/ PARAMETERS	Acquisition Time (sec)	Orientation	Resolution Matrix	FoV Read	FoV Phase	Number of slices	Slice thickess (mm)	Slice gap (mm)	Repetition time (msec)	Echo time (msec)	Flip angle (deg)	Fat suppression	Flow compensation	averages
Localizer	18	transversal coronal	179*256	430	100	15	6	9	1200	91	160	No	No	1
T2 coronal	175	coronal	288*320	300	100	35	5	0	2000	91	160	No	No	1
TriFi coronal	19	coronal	256*256	377	100	34	5	0	570	1.68	52	No	No	1
Cinematic TruFi	16	coronal	289*288	380	100	3	3	0	523	1.86	60	No		1
TruFi axial	19	axial	206*256	380	80.5	50	5	0	382.48	1.68	50	No	No	1
T2 axial	60	axial	203*320	331	78.1	35	5	1	1600	95	160	No	No	1
T2 Fatsat axial	60	axial	203*320	331	78.1	35	5	1	1600	95	160	No	No	1
VIBE Dixon coronal pre and post gard arterial portal venous	18+ 18	coronal	234*320	426	81.3	144	1	0	4.23	1.35	9	Yes		1
T1 VIBE Axial	15	Axial	182*320	380	81.3	72	3	0	3.31	1.3	9	Yes		1
DWI with b value of 50, 400, 800	232	transverse	108*134	380	80.6	30	5	2.5	5700	48		Yes	1	

be instructed to drink the solution gradually for even distension of the entire small bowel.

One hour after the commencement of oral contrast ingestion patient will be imaged on **MAGNETOM SKYRA 48 channel 3 TESLA MR Machine by Siemens, Germany** using phased array abdomen coil in supine position. Patient will be instructed for breathing instructions.

After running the kinematic sequences and just before iv contrast enhancement sequences 1mg of i.v buscopan each will be given to minimize movement artifact from peristalsis. Images are obtained.

STUDY DESIGN

This is a longitudinal prospective study.

STATISTICAL ANALYSIS:

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OUTCOME:

- MR Enterography will be performed in patients with clinically diagnosed Crohn's disease. The potential of MR Enterography to complement endoscopic, biochemical and other radiological modalties and to serve as a biomarker of disease activity will be evaluated.
- The correlation of DW sequence findings to contrast enhanced sequence findings will be done which can help to assess the potential of DW sequence to replace contrast enhanced sequence specially in pregnant and renal function compromised patients.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Sr. No.

Name:

Age and sex:

MRD number:

Address:

Contact number:

HISTORY:

1. Diarrhoea and frequency of loose stools
2. Blood in stools
3. Abdominal pain
4. Fever
5. Vomiting
6. Fatique / general well being
7. Anti diarrhoeal drug use
8. Arthritis / Arthralgia
9. Iritis/ Uveitis
10. Skin / mucosal symptoms
11. Anal fissure, fistula or abscess

PAST HISTORY:

INVESTIGATION:

1. Ultrasound abdomen
2. Upper GI endoscopy findings if any
3. Lower GI endoscopy findings if any
4. Serum creatinine
5. TLC
6. Hemoglobin
7. ESR
8. CRP
9. Faecal calprotectin / lactoferrin
10. CT enterography if any: photocopy to be attached
11. HPE :

Signature of Candidate **Signature of Supervisor**

MR ENTEROGRAPHY FINDINGS:-

BOWEL DISEASE LOCATION FINDINGS				
NUMBER OF DISEASE SEGMENTS				
T2 HYPERINTENSITY				
ENHANCEMENT PATTERN				
INTRAMURAL EDEMA AND WALL THICKENING				
DIFFUSION RESTRICTION				
ULCERATIONS				
FIBROSIS OR STRICTURES				
UPSTREAM DILATATIONS				
CALIBRE AND PLIABILITY				
PERISTALSIS				
MESENTERIC FINDINGS				
PENETRATING COMPLICATIONS				

Signature of Candidate **Signature of Supervisor**

EXTRAINTESTINAL FINDINGS IF ANY:

FINAL MR ENTEROGRAPHY IMPRESSION

SURGICAL HPE FINDINGS

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... .....am willing to participate in the study **"PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

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गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫ਼ਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"PROFILE OF MR ENTEROGRAPHY IN CROHN'S DISEASE" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ